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MULTIPLE-BALLOON KYMOGRAPH RECORDING OF THE ACTION OF SYNTROPAN AND OF TRASENTIN ON THE MOTILITY OF THE UPPER SMALL INTESTINE IN MAN

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SINCE differences of opinion have arisen concerning the claims that syntropan (phosphoric acid salt of the tropic acid ester of 3-diethylamino-2, 2-dimethyl-1-propanol) and trasentin (diphenylacetyl-diethylaminoethanol hydrochloride) have an effective relaxing action on the motility of the gastrointestinal tract, we have included these two synthetic agents in the course of a series of studies of drugs that allegedly influence the motor activity of the small intestine in man.

Clark and associates, in 1939, concluded that syntropan depressed the activity of the duodenum in the unanesthetized dog with fewer side effects on heart rate, pupillary size, and salivation than is noted with the use of atropine. It was regarded as having a direct effect on the smooth muscle and possibly a parasympatholytic action as well (7, 8). Jackman and Bargen observed that this agent when given intravenously in humans, inhibited "tone" and contractions of the unstimulated intestine. The action of syntropan was found to be comparable to that of atropine, but with fewer side effects. More recently, Posey, Bargen, Dearing, and Code obtained no intestinal effect or side reactions in doses of 100 milligrams of syntropan given orally to patients (13). Similar data on the ineffectiveness of syntropan on the motility of the human gastrointestinal tract have been presented by Atkinson and associates; Kramer and Ingelfinger; and Lorber and Machella. According to Lorber and Machella syntropan, given intravenously in doses of 10 to 25 milligrams, decreased tonus, abolished contractions, and retarded transport of the balloon in the stomach and intestine in human subjects. The duration of the drug action, however, was brief, varying on an average from 3 to 17 minutes. No effects on motor function of the intestine were obtained by subcutaneous or intestinal infusion of the drugs, although undesirable side effects were noted when syntropan was given intravenously or subcutaneously.

Early studies involving trasentin revealed that this drug diminished or abolished "spasms" and contractions of the small and large intestine induced by various drugs or by vagal stimulation in anesthetized dogs (12). When tested intravenously in a dosage of 50 milligrams in colostomy patients, its spasmolytic properties were regarded as more effective than those of atropine and without the undesirable side effects of the latter (9). The local application of trasentin to the intestine of the dog suggested that the smooth muscle

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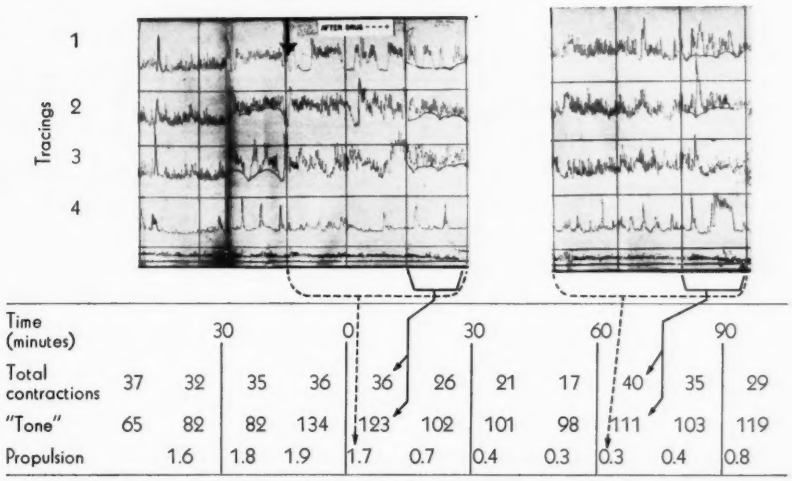
relaxing effect of the drug might, in part, be attributed to its anesthetic action on the sensory receptors of the bowel wall (6). Of particular importance have been the observations of Atkinson, Adler, and Ivy in dogs and in the human (1). They found that trasentin, by whatever route administered, was, along with atropine, the best depressant of spontaneous colon motility among the drugs studied by them. Furthermore, this agent was said to improve co-ordination between segments and to establish a gradient or type of motor pattern in the colon conducive to propulsion (1). Later reports tend to modify the earlier enthusiasm for trasentin. Recently, Posey and associates studied the effect of the oral administration of 75 to 150 milligrams of the drug in 5 patients, 1 with an ileal stoma and 4 with a colonic stoma. No effects were observed in 4 cases. In the fifth, motility was not modified, but tone was increased slightly. According to Kramer and Ingelfinger, the action of 50 milligrams of trasentin given parenterally was about 30 per cent as effective as 0.6 milligram of atropine administered subcutaneously. While the various workers support the original claim that trasentin in therapeutic doses has few or no side effects, the reports concerning its inconsistencies as a so called antispasmodic agent necessitate further study.

In studies of the motility of the upper small intestine in man we have tested the action of syntropan on the duodenum and upper jejunum in 4 healthy subjects and of trasentin with 4 observations in 3 human subjects. Two subjects were given 30 milligrams of syntropan intramuscularly. Two other subjects were given 50 milligrams of syntropan—one orally and the other by direct infusion into the duodenum. The results in the 2 subjects receiving oral syntropan were compared to the effects of placebos and 0.4 cubic centimeter of tincture of belladonna. In 1 of the subjects receiving syntropan intramuscularly the action was compared to atropine, 0.6 milligram, given by the same route. Two of the subjects on whom the action of trasentin on the upper small intestine was tested were healthy adults and 1 was a 54 year old patient with a complaint of epigastric pain which came on within a year following a cholecystectomy for cholelithiasis. At the time of the study this patient was asymptomatic. All 3 subjects were given 150 milligrams of trasentin orally. One of the subjects was also tested with an intramuscular injection of 50 milligrams of the drug. In the 2 healthy subjects, the action of trasentin was compared to the changes in motor activity after the administration of placebos. Motility in response to both syntropan and trasentin was recorded graphically with a multiple-balloon water manometer system and the effect of the agents was noted on propulsive and nonpropulsive contractions and on "tone." These various phases of motility have been defined elsewhere (2, 3, 4).

METHOD

The recording technique and the procedure of assessing the motility tracing patterns have been described (2, 3, 4). In brief, the procedure consisted of placing the 4 lumen tube with 4 balloons attached at intervals of 4 inches into the upper small intestine by fluoroscopic control. The subjects remained in a fasting state throughout the tests. The agents were given after an average control period of 61 minutes, with a range from 42 to 102 minutes. The duration of the average post-drug periods were as follows: oral syntropan, 113 minutes; syntropan given intramuscularly, 65 minutes; trasentin, 200 minutes; tincture of belladonna, 240 minutes; atropine given intramuscularly, 75 minutes; and the placebos, 214 minutes.

Propulsive contractions were assessed by visual inspection of the graphic records, taking into account the height and frequency of the contractions. The mean of the sum of the average values, expressed in arbitrary units, of the individual balloon tracings for each 15 minute interval was then determined. Variations in nonpropulsive contractions could not readily be reduced to numerical values, hence, only their general trend within gross limits was noted (2, 3). The mean "tone" levels during the "spasm"-free intervals were determined by measuring with a centimeter ruler the average distance between the resting level of contractions and the baseline of the tracing per 5 minute period. In addition,



Time (minutes)	30		0		30		60		90	
Total contractions	37	32	35	36	36	26	21	17	40	35	29
"Tone"	65	82	82	134	123	102	101	98	111	103	119
Propulsion		1.6	1.8	1.9	1.7	0.7	0.4	0.3	0.3	0.4	0.8

Fig. 1. Sections of graphic record of the variations in motility of the upper small intestine before and after the oral administration of 50 milligrams of syntropan. The changes in the levels of total contractions, "tone," and propulsion are indicated below the graph. Total contractions and "tone" were determined by surface area measurements of the tracings for each 5 minute period just previous to each 15 minute interval, and were expressed in square centimeters. Propulsion values represent the average of 15 minute interval and are expressed in arbitrary units. The graph shows that, as propulsive contractions were decreased, nonpropulsive contractions became more prominent after the drug was given. The values below the graph indicate that total contractions were decreased relatively less than nonpropulsive contractions throughout the postmedication period shown by the tracings. "Tone" was seen to vary but with a tendency to increase as compared to the control period.

changes in "tone" and total contractions were calculated by measuring the surface areas of the tracings representing these 2 components of motility for 5 minutes previous to each 15 minute interval in subject No. 1 receiving syntropan. The action of the agents was then compared at half-hour intervals to the average "tone" levels during the 45 minute control period preceding the administration of the agents and were expressed as percentage changes.

In the syntropan studies, with the exception of the test in subject No. 2, when only 1 balloon was in the small intestine, all the recordings of intestinal activity were made with from 2 to 4 balloons. In the trasentin studies 3 tests were carried out with the first 3 balloons and 1 test with 4 balloons, in the duodenum and upper jejunum.

The recording of respiration, blood pressure, and pulse rate and the technique of eliciting side reactions have been described previously (2, 3, 4).

RESULTS

Oral syntropan, 50 milligrams

The graphic record of the changes in motility of the duodenum and upper jejunum before and after the administration of 50 milligrams of syntropan orally to subject No. 1 is shown in Figure 1. The top, or No. 1, tracing is a record of activity from the proximal jejunum; the No. 2 tracing, from the region of the ligament of Treitz; and the No. 3 tracing, shows the motor activity in the duodenum. The No. 4 tracing is a recording from the stomach and was not used in the evaluation of the drug. The values for the changes in motility are shown below the graphic record.

Effect on contractions. The medication was given after a 50 minute control period. About 10 minutes later, propulsive contractions (high, sustained waves) began to fall off and remained about 75 per cent less than during the control period, starting at the 24 minute and extending to the 90 minute postdrug

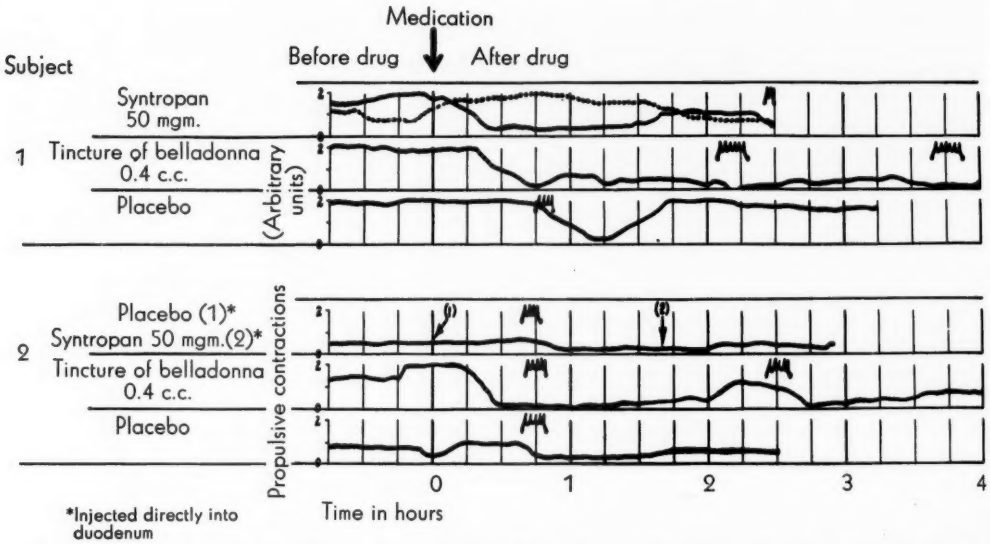


Fig. 2. The figure shows that in subject No. 1 syntropan diminished propulsive but not nonpropulsive contractions. In subject No. 2 the drug produced no diminution in propulsive contractions. In contrast, the tincture of belladonna produced a definite decrease in propulsion. The changes in propulsive contractions following placebo administration were more comparable to the syntropan effects. The short wavy line indicates "spasm"; the black line, propulsive contractions level; the interrupted line the nonpropulsive contractions level.

interval. Thereafter, propulsive contractions increased to within nearly 45 per cent of the average level of activity before the drug was given. Absolute values for the changes in propulsive contractions are shown in Figure 1. While propulsive contractions diminished, there was at the same time an increase in nonpropulsive contractions (lower, rapid waves) as shown graphically in Figure 2. Nonpropulsive activity decreased again at the time when propulsive contractions partially recovered. The net effect of the drug on contractions can be seen from the square centimeter surface area measurements of total contractions (propulsive and nonpropulsive) shown in Figure 1. Total contractions decreased about 40 per cent during the 30 to 60 minute postdrug interval and then returned to the control level. While total contractions, and propulsive contractions in particular, decreased, we hesitated to call this drug effect comparable to that produced by either oral atropine or tincture of belladonna. These belladonna alkaloids act by decreasing all contractions. In this subject tincture of belladonna, 0.4 cubic centimeter, produced a more lasting effect on propulsive activity (Fig. 2). A similar decline in activity was also observed in nonpropulsive contractions during the tincture of belladonna test. The percentage decrease in total contractions following the administration of tincture of belladonna is shown in Table I. The reduction in activity ranged from 17 to 77 per cent throughout the 4 hour observation period. The temporary decline in propulsive movements in this patient's placebo study was associated with the spontaneous occurrence of a "spasm" or temporary marked increase in "tone" which is indicated by the "saw-toothed" figure just after the 45 minute postdrug interval (Fig. 2). The maximal decrease of 47 per cent in total contractions during the placebo study was 3 per cent more than the maximal decline in total contractions noted with syntropan (Table I).

Effect on "tone." "Tone," as estimated for each 5 minute period by a centimeter ruler and as expressed in percentage changes per half-hour period, was found to increase from 12 to

TABLE I.—RELATIVE EFFECTS OF SYNTROPAN, TINCTURE OF BELLADONNA, ATROPINE AND PLACEBOS ON CONTRACTIONS AND "TONE" OF UPPER SMALL INTESTINE

Subject number	Agent and dosage	Motility phase	Percentage changes during postmedication period							
			Time in minutes							
			30	60	90	120	150	180	210	240
1	Syntropan 50 mgm. P.O.	Total contraction¶	−9	−44	+15					
		Tone*	+28	+12	+24	+36	+42			
	Tincture belladonna 0.4 c.c.	Tone*	+ 8	−16	−16	−24	−24	−21	−21	−15
		Total contraction	−17	−65	−72	−72	−85	−62	−65	−77
		Tone†	+ 5	−24	−30	−34	− 4	−26	−15	− 7
	Placebo	Tone*	+21	+21	+17	+24	+37	+37		
		Total contraction	− 7	−37	−47	+20	+ 8	−15		
		Tone†	+24	+25	+13	+43	+53	+45		
2	Syntropan 50 mgm.‡	Tone*	+11	+33						
	Tinct. belladonna 0.4 c.c.	Tone*	−18	−25	−23	−20	−23	−25	−26	−27
		Total contraction	−48	−52	−81	−57	−29	−86	−52	−43
		Tone†	−10	−18	−36	−59	− 5	−35	−35	−24
	Placebo	Tone*	−10	−10	−18	− 7				
3	Syntropan 30 mgm. I.M.	Tone*	+18	+18						
	Atropine 0.6 mgm. I.M.	Tone*	−40	−57						
4	Syntropan 30 mgm. I.M.	Tone*	− 5	− 8						

¶ Total contractions were measured only through the first 90 minutes of the postmedication period.
* "Tone" was determined during "spasm"-free intervals.
† "Tone" was determined as sq. cm. measurements of surface areas beneath resting levels of contractions per 5 minute period previous to each 15 minute interval.
‡ Syntropan was injected through one channel of the tube directly into the duodenum.

42 per cent after syntropan was given, which is comparable to the increase in "tone" in this subject's placebo study (Table I and Fig. 1). In square centimeters the variation in "tone" was from plus 17 to plus 37 per cent. In contrast, tincture of belladonna decreased "tone" from 15 to 24 per cent according to the centimeter scale measurements and from 4 to 34 per cent according to the more elaborate measurements of surface area of the tracings representing "tone." Thus, "tone" increased after the administration of syntropan to a degree comparable to that noted in the placebo test, whereas "tone" was reduced following the administration of tincture of belladonna.

Syntropan, 50 milligrams, injected into duodenal lumen

In subject No. 2. 50 milligrams of syntropan, dissolved in 50 cubic centimeters of water, was injected directly into the duodenal lumen.

Effect on contractions. As shown in Figure 2, propulsive contractions increased in 20 minutes and remained elevated for the rest of the 75 minute observation period. Earlier in this test the injection of a comparable amount of water was followed by no change in contractions until 50 minutes later when the decrease in activity was associated with the occurrence of a "spasm." It is of interest to note that when this subject was given a placebo in another test, shown by the bottom graph in Figure 2, the variations in propulsive contractions were remarkably similar to those in the test just described. A "spasm" and a decrease in propulsive movements occurred at the 40 minute postdrug interval in both placebo tests. Activity increased again about 25 minutes sooner in the placebo study than in the combined placebo-syntropan test. In both studies the duration of the control period was 45 minutes. This subject obtained a striking decrease in propulsive activity within

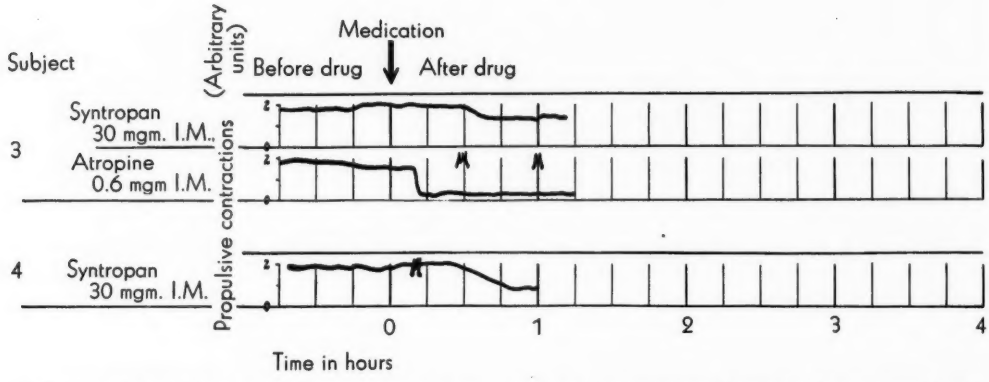


Fig. 3. The figure shows that while a diminution in propulsive contractions occurred in 30 minutes after the intramuscular injection of 30 milligrams of syntropan the effect was much less pronounced than after the intramuscular injection of atropine, 0.6 milligram. The short wavy line indicates "spasm"; the black line, propulsive contractions level.

30 minutes after the administration of the 0.4 cubic centimeter of tincture of belladonna. The duration of the control period in this test was 45 minutes and again a "spasm" occurred at the 40 minute postdrug interval. But in this instance, the decrease in propulsive activity preceded rather than occurred in association with the "spasm." We concluded that the direct infusion of 50 milligrams of syntropan directly into the duodenum was without effect on propulsive movements. Changes in nonpropulsive activity were similar to those in propulsive contractions.

Effect on "tone." "Tone" became elevated as much as 33 per cent after the direct infusion of syntropan into the duodenum (Table I). During the placebo test "tone" was slightly decreased but to a less extent than following the administration of 0.4 cubic centimeter of tincture of belladonna. In this latter study "tone" was consistently diminished from 18 to 27 per cent according to the centimeter scale measurements and from 5 to 59 per cent according to the surface area determinations of changes in "tone."

Syntropan, 30 milligrams, given intramuscularly

Effect on contractions. In subjects Nos. 3 and 4, the intramuscular injection of 30 milligrams was followed by a decrease in propulsive contractions in about 30 minutes, the effect being more marked in No. 4 than in No. 3. As no control studies were done in these subjects, we were unable to say whether this response represented a drug effect. It was evident, however, that its action was less than the effect of the intramuscular injection of 0.6 milligram of atropine noted in subject No. 3. Atropine produced a marked fall in propulsive contractions after a 10 minute latent period. This maximal action was maintained for the remainder of the 75 minute period. In these 3 tests nonpropulsive contractions changed in the same direction, although the action of atropine was the more pronounced on propulsive activity.

Effect on "tone." As shown in Table I, "tone" was increased on an average of 18 per cent in subject No. 3 and diminished on an average of 7 per cent in subject No. 4 after giving syntropan. Atropine, on the other hand, lowered "tone" from 40 to 57 per cent in subject No. 3. We concluded that syntropan given intramuscularly had no appreciable relaxing effect on "tone" in these 2 subjects.

Trasentin

A graphic record of the test in subject No. 1, which was typical of our findings with trasentin, is shown in Figure 4. Tracings Nos. 1, 2, and 3 represent the activity of the upper jejunum and duodenum. Tracing No. 4 is a recording of stomach activity and was not used in evaluating the drug. After a 70 minute control period, 150 milligrams of trasentin

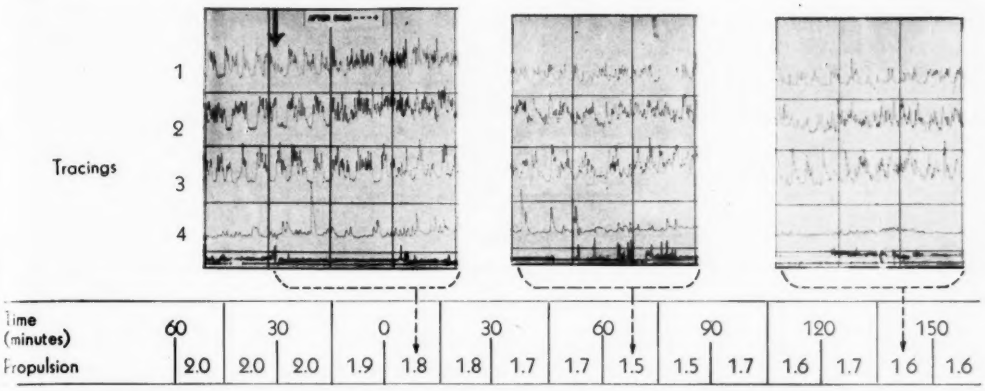


Fig. 4. Sections of graphic record of the motility of the upper small intestine before and after the oral administration of 150 milligrams of trasentin. The tracings are from the following locations in the upper small intestine: No. 1, proximal jejunum; No. 2, proximal jejunum or distal portion of the duodenum; No. 3, duodenum; No. 4, stomach (not used in assessing the effect of the drug). As shown by the average values per 15 minute period, as indicated below the graph sections, propulsive contractions decreased only slightly and gradually after the administration of trasentin. The decline in activity was principally in the No. 1 tracing. The drug had no effect on propulsive contractions.

were given orally. It can be seen from the figures below the record which indicated the average changes in propulsive contractions for each 15 minute period, that propulsive activity declined only slightly and gradually with the passage of time. This decrease in activity was most noticeable in the No. 1 tracing of jejunal contractions. We concluded that contractile activity was not appreciably altered by the drug throughout this observation period. The variations in "tone" will be mentioned later.

Effect on propulsive contractions. In Figure 5, the summary values for the trasentin and placebo tests are shown in graphic form for each subject. After subject No. 1 received 50 milligrams of trasentin intramuscularly, there was little or no decline in propulsive contractions until the start of the second hour of the postdrug period. Thereafter, propulsive contractions declined slowly so that 1 hour later they were about 46 per cent less active than during the control period. For the next 82 minutes the slow decline in propulsive activity continued. The record of this subject's test with 150 milligrams of oral trasentin has already been shown in Figure 4. When this study, the one just described, are compared to the placebo test in this subject, it can be seen that the action of trasentin on propulsive contractions differed very little from that of the placebo for the first 75 minutes. During the remaining observation periods the decline in activity with oral trasentin was less, and with intramuscular trasentin, more than that noted in the placebo study. However, because nearly 85 minutes had elapsed before contractions decreased with intramuscular trasentin, we felt that this decline in activity did not represent a drug effect. A comparison of subject No. 2's placebo test and the one in which he received 150 milligrams of trasentin orally revealed very little difference in the two studies. If anything, the decline in propulsive contractions in the placebo test was the more striking. Subject No. 3 received 150 milligrams of trasentin orally. Little or no decrease in propulsive contractions was observed over a 140 minute period.

When the results in 8 subjects who were also tested with placebos were compared with the findings after the administration of atropine given orally or of tincture of belladonna, there could be little doubt of the ineffectiveness of trasentin in reducing propulsive contractions. Both tincture of belladonna, 0.4 cubic centimeter, and oral atropine, 0.45 to 0.6 milligram, produced a sustained diminution in propulsive contractions of 71 per cent as compared to an average decrease of 31 per

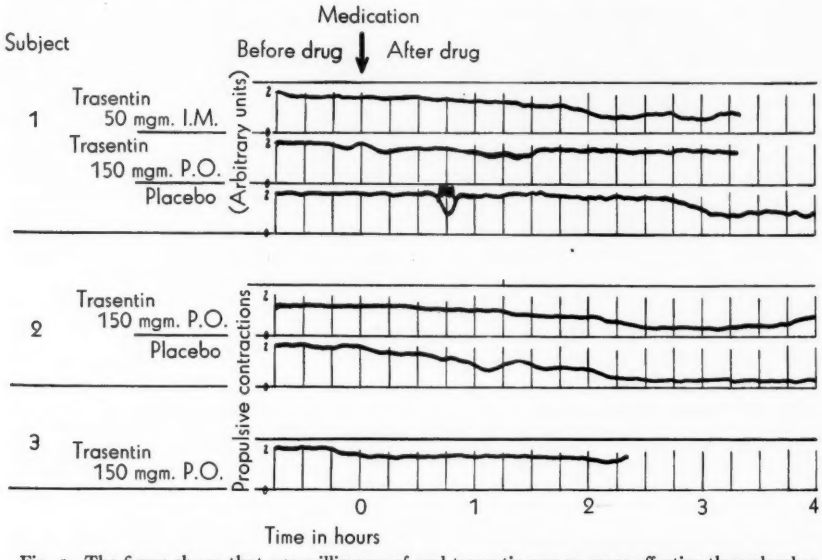


Fig. 5. The figure shows that 150 milligrams of oral trasentin was no more effective than placebos in decreasing propulsive contractions. The diminution in activity noted 90 minutes after the intramuscular injection of 50 milligrams of trasentin was regarded as too late an effect to be considered a drug action. The short wavy line indicates "spasm"; the black line, propulsive contractions level. The heavy-black line represents the level of propulsive contractions in arbitrary units throughout the observation periods. The "saw-toothed" figure indicates the time and duration of a "spasm" or sudden temporary increase in "tone" in the placebo test of subject No. 1.

cent following the administration of placebos (4). With these belladonna alkaloids, moreover, the maximal effect was obtained in from 25 to 40 minutes with the exception of 2 tests in which these agents appeared to be ineffective.

The effect of the drug on nonpropulsive contractions was, so far as could be determined, no different than that observed on propulsive contractions.

Effect on "tone." As shown in Table II, "tone" during "spasm"-free intervals varied from subject to subject as well as from one half-hour period to another in a given individual after both trasentin and placebos were administered. There was an overall increase in "tone" in both groups of tests indicating that trasentin did not diminish "tone." Moreover, when motor activity recorded by individual balloons was considered, there was no instance of a decrease in "tone" in any bowel segment following trasentin administration. Tincture of belladonna, 0.4 cubic centimeter, on the other hand, produced a slight but consistent decrease in "tone" during "spasm"-free intervals. This decrease in "tone" averaged minus 18 per cent with a range from minus 10 to minus 21 per cent for the 45 to 240 minute postmedication period in 9 studies (4). Five subjects receiving orally 0.4 to 50.6 milligram of atropine showed no consistent change in "tone."

Side effects

Neither syntropan nor trasentin produced any definite alterations in respirations, blood pressure, or pulse rate. Although moderate dizziness was noted by the 2 subjects who were given syntropan in the oral form, no other symptoms were complained of which could be ascribed to the administration of either syntropan or trasentin.

DISCUSSION

Eight observations have been made of the action of syntropan and of trasentin on the motility of the upper small intestine in man. The effects of the drugs were noted on propulsive and nonpropulsive contractions and

TABLE II.—INDIVIDUAL AND MEAN VALUES SHOWING PERCENTAGE CHANGES IN "TONE" DURING "SPASM"-FREE INTERVALS AFTER ADMINISTRATION OF TRASENTIN AND PLACEBOS*

Subject number	Agent given	Percentage changes in "tone" after agents were administered							
		Time in minutes							
		30	60	90	120	150	180	210	240
1	Trasentin 50 mgm. I.M.	+10	+12	+19	+24	+16	+16	+16	
	Trasentin 150 mgm. P.O.	+12	+11	+11	− 2	0	+ 7	+ 7	
	Placebo	+ 5	+ 2	+ 2	+ 7	+ 2	+16	+19	+19
2	Trasentin 150 mgm. P.O.	+10	+14	+17	+22	+29	+36	+31	+40
	Placebo	+ 5	+ 5	+ 5	+ 5	+17	+24	+30	+30
3	Trasentin 150 mgm. P.O.	+30	+52	+75	+84				
Mean	Trasentin 150 mgm. P.O.	+17	+26	+34	+35	+15	+22	+19	+40
	Trasentin 50 mgm. I.M.	+10	+12	+19	+24	+16	+16	+16	
	Placebos	+ 5	+ 4	+ 4	+ 6	+10	+20	+25	+25

*Percentage changes in "tone" were determined in each test by dividing the average "tone" value for each 30 minute postmedication period by the average "tone" value for the last 45 minutes of the control period.

"tone," which were recorded graphically with a multiple-balloon water manometer system.

Two subjects received syntropan in a dosage of 50 milligrams. In one instance, this drug was given orally; and in the second subject, was injected directly into the duodenum. Two additional subjects were given 30 milligrams of syntropan intramuscularly. The results of these 4 studies of the effect of syntropan on motor activity were compared to the changes in motility occurring following the administration of tincture of belladonna, 0.4 cubic centimeter, and placebos in 2 subjects, and following the intramuscular injection of 0.6 milligram of atropine in 1 subject.

Syntropan definitely produced no decrease in "tone" when given either orally or intramuscularly. The giving of the drug orally was followed by a 75 minute decrease in propulsive contractions in 1 subject. Since this decrease in activity was associated with a rise in nonpropulsive contractions, it was questionable whether this observation represented a true drug effect comparable to that noted with the belladonna alkaloids. Both oral atropine and tincture of belladonna were found to decrease both propulsive and nonpropulsive contractions (4). When syntropan was given intramuscularly, a slight to moderate decrease in propulsive contractions occurred in 30 minutes. While this result may have represented some effect of the drug, it was less than that obtained with 0.6 milligram of atropine given intramuscularly to subject No. 3.

Because of differences in the route of administration our results are only partially comparable to the findings of Posey and associates. These workers noted no effect nor side reactions from 100 milligrams of syntropan given orally in one patient with an ileal stoma, and in another patient with a colonic stoma. Our studies support their conclusions. The slight transient effect of the intramuscular injection of the drug appears similar to the essentially negative results obtained by Lorber and Machella with the subcutaneous administration of syntropan. Since syntropan is rarely used subcutaneously or intravenously, we wish to place greater importance on its effect as an oral medication.

These observations lead us to conclude that, so far as could be determined by employing the multiple-balloon technique in healthy subjects, syntropan has little or no effect on the motility of the upper small intestine. These studies do not exclude the possibility that the drug may have a favorable action on hypermotility or motor dysfunction. It seems more likely, however, that any clinical value derived from the use of syntropan must be due to some mechanism other than that of decreasing contractions and "tone."

In all 4 of the observations made of the action of therapeutic doses of trasentin on the

motility of the upper small intestine in man, there was clearly no effect of the drug on contractions or "tone" during the first hour. In 2 hours 1 of the 4 tests showed a 46 per cent decline in propulsive activity which was progressive for the remaining 82 minute observation period. We were inclined to feel that this diminution in activity represented a spontaneous decline rather than a drug effect. Of the 3 remaining studies, 1 subject showed definitely no change in contractions in 142 minutes, while the changes in the other 2 tests were about the same as those obtained with placebos in the same subjects. "Tone" increased slightly more with trasentin during "spasm"-free intervals than in these patients' placebo tests as well as in other studies with placebos.

These results are similar to the recent findings of Posey and associates and Kramer and Ingelfinger which emphasized the relative ineffectiveness of trasentin as an "antispasmodic" agent (10, 13). As our subjects were all symptom-free when studied, the observations did not test the effect of the drug on gastrointestinal symptoms. It may be, as suggested by Crohn and his associates, that the favorable influence of trasentin on symptoms is due to a local anesthetic action on the bowel wall. Another possible explanation for its therapeutic benefits may be that it favorably modifies hypermotility or motor dysfunction responsible for gastrointestinal complaints. Atkinson, Adler and Ivy's findings showing that more effective propulsion was obtained in the colon following trasentin administration is suggestive of this latter possibility. We did not test this hypothesis for, so far as we were aware, our tracings did not contain graphic evidence of either hypermotility or inco-ordination of adjoining bowel segments of the type that may give rise to symptoms. The point made by Atkinson and his associates is, however, a pertinent one and should be pursued further in studies on patients with known alimentary tract motor disturbances. In the light of our other motility studies we feel that the belladonna alkaloids remain the effective "antispasmodic" agents and that the action of trasentin on motility, as recorded by the multiple-balloon system, does not differ from the changes in motor activity noted with placebos (4).

SUMMARY

1. Multiple-balloon kymograph recording has been made of the action of syntropan and of trasentin on the motility of the upper small intestine in 7 human subjects. Two subjects received 30 milligrams of syntropan intramuscularly; 2 subjects were given 50 milligrams of syntropan, one orally and the other by injection into the duodenum. Three subjects received 150 milligrams of trasentin orally, and on another occasion, 1 of these subjects was given 50 milligrams intramuscularly. The action of syntropan was compared with the changes in motility following the administration of tincture of belladonna, 0.4 cubic centimeter, and atropine, 0.6 milligram given intramuscularly, and to the effect of the administration of placebos. Two of the subjects who received trasentin were also tested with placebos.

2. There was no evidence that syntropan caused a decrease in contractions or "tone" comparable to that noted with tincture of belladonna or atropine nor that propulsive or nonpropulsive contractions were decreased to a greater degree in response to trasentin than following the administration of placebos. Moreover, there were indications that trasentin was ineffective in diminishing "tone," since there was an overall increase in "tone" concurrent with the passage of time.

3. It is conceivable that any clinical value derived from the use of syntropan or trasentin may be due to the action of the drugs on hypermotility or motor dysfunction, although the effects of syntropan and trasentin on such abnormal motor disturbances were not studied. The fact that these drugs may have a favorable effect on gastrointestinal symptoms through a local anesthetic action on the bowel wall has been discussed.

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A METHOD FOR CONTROL OF POSTOPERATIVE PAIN

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FEAR of death and fear of pain often account for failure to obtain permission to perform necessary and sometimes lifesaving elective operations. Sensible and understanding discussion with the patient concerning the risks of the procedure will usually ease or erase the apprehension of death. Pain, however, cannot be controlled successfully by conversational reassurance. The universal use of morphine, morphine-like drugs, and other analgesics has reduced the suffering following operations. These drugs, however, have undesirable side actions, particularly when employed in excess. Depressions of respiratory functions in patients who have had operations or injuries of the chest are an important and common problem. The proper management of postoperative medication in older patients may also be difficult. An easy and apparently safe method for the control of pain following operations on the chest has been employed at the George Washington University Hospital.

METHOD

At the completion of an operation on the chest, small plastic tubes[1] are placed at the inferior border of four ribs or, if a rib has been removed, the posterior stump of the rib in a position anterior to the erector spinae muscle. A small tunnel can be made in the intercostal muscle for a distance of 1 or 2 centimeters at the point at which the tube is anchored posteriorly. A few fine silk or catgut sutures are employed to hold the tubes in place, and the erector spinae muscle is placed over the distal end of the tube (Fig. 1). It has been found convenient to bring the tubes out at the anterior angle of the wound. This position makes injections through the tubes easier and the patient is not annoyed by having to be turned when the medication is given (Fig. 4).

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[1]Aeroflex tubing, measuring .043 inch by .068 inch.

Two cubic centimeters of either 1 per cent or 2 per cent procaine solution are injected through the tubes every 3 hours. With a few patients it has seemed desirable to inject the medication at 2 hour intervals. This can be done without changing the position of the patient. Since the caliber of the tube is small, injections accomplished by inserting a needle into each tube, although not difficult, are somewhat time-consuming and troublesome.

A simple apparatus has been devised which makes it possible to use a single syringe filled with procaine and all of the outlets can be reached quickly and without disturbance of the individual tubes (Figs. 2 and 3).

RESULTS

Subjective results. Thirty-six patients have been observed, 18 of whom were employed as controls and treated by the usual accepted medications for control of pain. In the other 18 cases plastic tubes were placed in the wounds and injections of 2 cubic centimeters of 1 per cent or 2 per cent procaine employed at 2 to 4 hour intervals. It is important to emphasize that in the group of cases in which the plastic tubes were used there was no change in orders for postoperative medications. Moreover, the nursing staff was not instructed to withhold medications and, in most instances, the nurses did not know that an evaluation of a technique was in progress. Table I shows the individual and total amounts of morphine given in the two series.

It is not surprising that there is wide variation in individual cases and it should be noted that some of the operations were more severe than others. The difference in total medication, however, seems significant.

Since there was no effort to withhold morphine and undoubtedly it was given on occasions for the euphoria that might be produced, the gratifying relief from the injection of procaine through the plastic tubes is not so

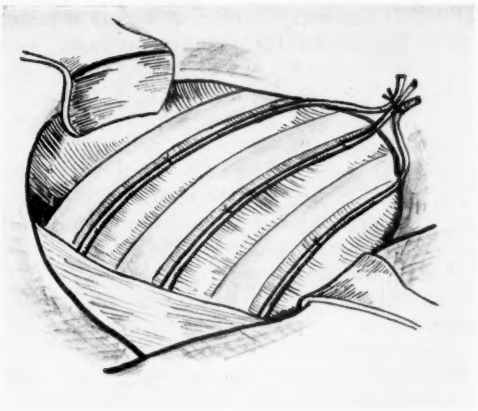


Fig. 1. Surgical wound of the chest with plastic tubes in place.

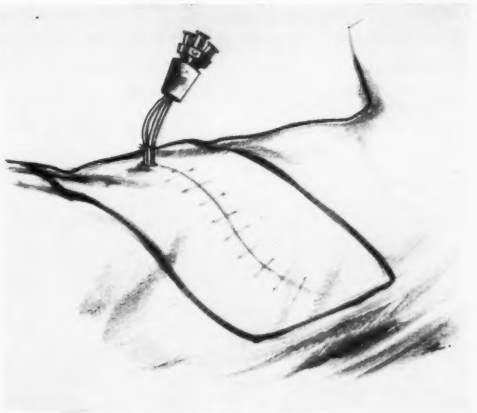
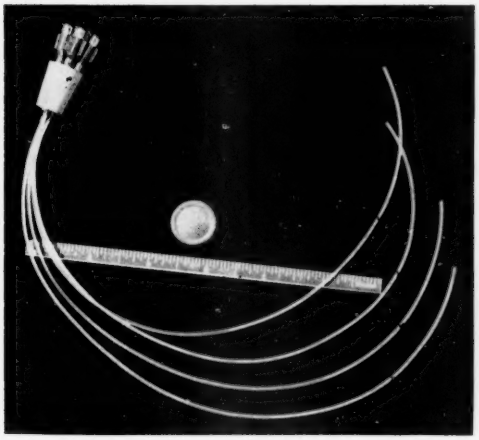


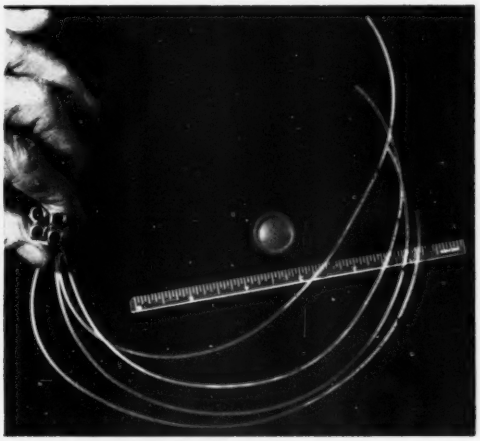
Fig. 4. Anterior position of the tubes and delineation of zone of analgesia, as determined by skin resistance tests.

dramatically demonstrated on a comparison of total or individual medications.

In the series of 18 patients, the following subjective reactions prevailed. About 10 minutes after the injection of 2 cubic centimeters of procaine into each tube there is relief of severe pain, a sensation of stiffness and soreness and a backache remained, but the patient is able to move about in bed and this is particularly noticeable when, in the course of early ambulation, the patient is asked to move from his bed to a chair. There were no disagreeable side effects.

The tubes were left in the wounds from 3 to 9 days. At the end of 9 days all of the tubes were open. In this case the tubes were left in place longer than necessary to test their patency. Experience indicated that, after 4 or 5 days, reduction in postoperative pain and discomfort will usually allow discontinuance of the technique. There were no wound infections, nor was there difficulty in wound healing.





Figs. 2 and 3. Number 19 needles, which are 1½ inches in length, are fitted through a cork. The needle points are filed off and the plastic tubing is placed over the needles. The rubber cap which is shown in the photograph may be sterilized and placed over the needles between injections.

TABLE I.—MILLIGRAMS OF MORPHINE USED IN 7 DAY POSTOPERATIVE PERIOD

With plastic tubes	Mgm.	Without plastic tubes	Mgm.
1. Esophageal exploration	140	Lobectomy	59
2. Pulmonary denervation	240	Lobectomy	252
3. Lobectomy	110	Pneumonectomy	154
4. Thoracotomy and biopsy	130	Lobectomy	132
5. Excision of pulmonary cyst	55	Pulmonary denervation	160
6. Lobectomy	33	Excision of tuberculoma of lung	118
7. Esophageal exploration	110	Excision of tuberculoma of lung	47
8. Lobectomy	77	Pneumonectomy	282
9. Lobectomy	99	Lobectomy	122
10. Ligation of pulmonary artery	127	Lobectomy	211
11. Excision of pulmonary cyst	55	Excision of pulmonary cyst	165
12. Pulmonary denervation	121	Lobectomy	96
13. Excision of neurofibroma of mediastinum	55	Lobectomy	191
14. Pulmonary denervation	33	Pulmonary denervation	312
15. Removal of thoracic lipoma	55	Lobectomy	125
16. Pneumonectomy	220	Lobectomy	264
17. Pneumonectomy	88	Excision of tuberculoma of lung	134
18. Excision of pulmonary cyst	75	Lobectomy	135
Total	1,823	Total	2,959

Objective results. The individual variation in tolerance to pain made it necessary and desirable to test the method by objective techniques. This was accomplished in two ways. First, measurements of electrical skin resistance employing the neurodermometer were accomplished after the injections of procaine through the tubing; and, second, tests with starch-iodine powder over the chest wall with delineation of the zone of analgesia, after causing the patient to sweat by application of a heat lamp. Figure 4 demonstrates the extent of analgesia after injection of procaine into four plastic tubes placed at the inferior border of the four ribs.

COMMENT

The method has been employed in a few abdominal incisions and appears to be helpful. It may be desirable, however, to alter the design of the tubes by placing perforations along the sides to obtain a spray effect in abdominal wounds. This, of course, is not necessary after operations on the chest because the procaine solution can be placed at the posterior extremity of the intercostal nerves. Alterations in the apparatus may be desirable in abdominal wounds and more study on the effects of wound healing in the abdominal wall are necessary before final conclusions can be made. It seems safe, however, to employ this technique after thoracic operations. Relief of severe pain can be predicted and it seems reasonable to assume that reductions in postoperative pulmonary complications might be expected. The method is easy and the results gratifying.

ANEURYSM OF THE HEPATIC ARTERY

Report of Two Cases and a Consideration of Surgical Treatment

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ISIDOR S. RAVDIN, M.D., Philadelphia, Pennsylvania

ANEURYSMS of the hepatic artery are rare. We have discovered only 87 instances reported in the literature and, of these, only 11 were diagnosed before death.[1] If clinicians were on the alert for the symptoms and signs of hepatic aneurysm, they should be able to recognize the lesion much more often. Only 3 patients with aneurysm of the hepatic artery are reported to have been cured—all 3 by ligation of the hepatic artery (6, 20, 21). The majority of ligations, however, have resulted in death from liver necrosis soon after operation, and most surgeons have avoided ligation for this reason.

A discussion of hepatic aneurysm is pertinent at this time because of recent developments that provide new means of attacking this disease. In recent years surgeons have successfully revived the use of venous (4, 18) and arterial (13) grafts for bridging defects in arteries. By the use of grafts or by the anastomosis of a contiguous artery to the distal end of the hepatic artery, it might be possible to prevent liver anoxia following resection of the aneurysm. Operations of similar magnitude are now being safely performed with the aid of modern anesthesia and supportive therapy.

A recent discovery that may simplify the problem is Markowitz's observation that penicillin prevents death following ligation of the hepatic artery in dogs. Without the antibiotics the operation is nearly always fatal. Large doses of the antibiotics may prevent death in the human following ligation of the hepatic artery. In this paper we report 2 additional cases of hepatic aneurysm, both diagnosed during operation and both treated unsuccessfully, and discuss some pathological and clinical features of the lesion.

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[1]Since 1946, when McNamara, Baker and Costich summarized the literature of hepatic aneurysm, 2 additional reports have appeared (11, 34).

CASE 1. C. M., a 63 year old white man, was admitted to another hospital in September 1947 complaining of fever, abdominal pain, and weakness. He was given a course of penicillin and subsequently discharged. Several weeks later he had an attack of "biliary colic" and gradually became jaundiced. Operation was performed in February 1948 at the same hospital. A mass the size of a golf ball was seen at the junction of the cystic and common ducts. The gall bladder was opened but no stones were found. A tube was sewn into the gall bladder and the abdomen closed.

Following operation cholangiography was carried out through the cholecystostomy tube and showed that the cystic duct was greatly dilated and completely obstructed. The patient became severely jaundiced and developed generalized itching and acholic stools. On March 3, 1948 he was admitted to the Hospital of the University of Pennsylvania on the service of Dr. I. S. Ravdin.

On admission his temperature was 98 degrees F. (37.7 degrees C.), pulse 88, respirations 24, and blood pressure 150/90. The liver edge was palpated 10 centimeters below the right costal margin, was rounded, and was moderately tender. The urine contained bile. The hemoglobin was 13 grams per 100 cubic centimeters; the leucocyte count was 8,700 per cubic millimeter, with 73 neutrophils, 21 lymphocytes, 4 monocytes and 2 eosinophils; the plasma chlorides were 103 milliequivalents per liter, the plasma proteins were 7.1 grams per 100 cubic centimeters; the van den Bergh reaction was: direct, biphasic, indirect, 28 milligrams per 100 cubic centimeters; the prothrombin level was 78 per cent of normal; cephalin flocculation was plus 1 at the end of 48 hours; thymol turbidity was 0.6 unit; thymol flocculation was plus 1; the Kohlmer and Kline serologic tests for syphilis were negative.

After 10 days of preparation with a high protein, high carbohydrate, low fat diet and vitamin K, the patient showed a rise in the prothrombin level to 98 per cent of normal. Exploratory laparotomy was performed (I.S.R.) on March 11 under spinal anesthesia. At operation the common duct was observed to be enlarged and flattened over a nonpulsating, cystic mass the size of an orange, which upon aspiration yielded bright red blood. The lesion was diagnosed

Fig. 1. Photograph of under surface of liver, showing the aneurysm of the hepatic artery in Case 1, located 7 centimeters from its origin from the aorta. The sac measured 5 by 3 by 2 centimeters and occluded the common bile duct.

as an aneurysm of the hepatic artery. During exploration of the common duct, the aneurysmal sac, which closely approximated the medial wall of the common duct, was inadvertently opened and bled vigorously. A pack of oxidized cellulose was used to check bleeding and over the pack a T tube was sutured into the common duct and the abdomen closed.

Five days postoperatively clear bile drained from the T tube. On the sixth day the patient complained of nausea and right upper quadrant pain, and fresh blood appeared in the drainage. He went rapidly into shock and was taken to the operating room, where blood was given intravenously under pressure and his abdomen opened (W. T. F.). The peritoneal cavity was full of fresh blood which spurted from a hole in the aneurysm large enough to admit the tip of the thumb. This opening was packed with oxydized cellulose and with gauze soaked in tincture of benzoin. The brisk arterial bleeding stopped and the abdomen was again closed. Three thousand cubic centimeters of blood were given during the operation.

Postoperatively the patient grew gradually worse, with a daily temperature elevation to about 101 degrees F. (38.3 degrees C.), which was unaffected by large doses of penicillin and streptomycin. On the second postoperative day the liver function tests were repeated and were essentially unchanged. Jaundice and pruritus continued, though bile still drained from the T tube. The urine remained dark, and although the urinary output was good, the blood urea nitrogen rose to 94 milligrams per 100 cubic centimeters. The serum proteins fell to 5.5 grams per 100 cubic centimeters. Increasing weakness progressed to lethargy and coma, and the patient died 11 days after the second operation.

Autopsy findings (12 hours after death, performed by J. L. G.): The lungs revealed terminal bronchopneumonia and mild pneumoconiosis on both gross and microscopic examination. The liver weighed approximately 1,500 grams and was extremely soft and friable (Fig. 1). The common duct could be traced from the ampulla of Vater for a distance of 10 centimeters toward the hilum of the liver where it ended in a mass of blood clot, packing, and friable foreign material (oxydized cellulose), occupying a thin-walled sac 5 by 3 by 2 centimeters into which the hepatic artery propria opened directly. Seven centimeters of hepatic artery intervened between the aneurysm and the aorta. Incision of the liver showed many pinkish areas of extreme softening interspersed with brown, boggy parenchyma. No sharply demarcated infarcts were noted. The gall bladder wall was thick and rough; the gall bladder contained whitish mucoid material. The cystic duct could be traced into the common duct; the common duct was drained by the T tube proximal to the aneurysm but was completely blocked by the aneurysm distal to the tube.

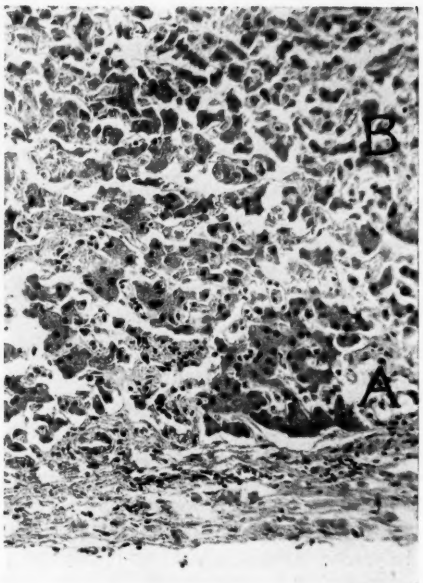

Fig. 2. Photomicrograph of liver in Case 1, showing extensive *in situ* parenchymal necrosis without signs of inflammation. Note line of demarcation between (*A*) living cells beneath capsule and (*B*) necrotic subjacent parenchyma. Viable cells are nourished by capsular vessels.

Microscopic examination showed that the perimuscular layer of the common duct was continuous with the adventitial layer of the aneurysmal wall. A well organized clot filled the sac, which had a thick intima containing cholesterol clefts and scraps of calcium. Throughout the liver widespread *in situ* necrosis was observed: the parenchymal cells had lost their nuclei and had a flat, opaque appearance. Empty spaces separated the necrotic cells. A few viable cells remained in some of the portal areas, and in a thin layer just beneath the capsule. (Fig. 2).

The aorta had numerous sclerotic plaques in the thoracic portion, increasing in the abdominal aorta, with calcification and ulceration of the posterior wall. There were no signs of syphilis.

The spleen weighed 280 grams. Microscopic examination showed calcification in the media of one of the larger branches of the splenic artery.

The kidneys weighed 210 and 180 grams and were enlarged, soft, and flabby. The cut surface was yellowish, and the architecture blurred. The cortices were normal in width and the pelves and ureters showed no lesions. On microscopic examination dense aggregations of bile pigment were seen in the distal convoluted and collecting tubules. Tubular epithelium was somewhat flattened but not necrotic.

Autopsy diagnoses were: arteriosclerotic aneurysm of the hepatic artery with occlusion of the artery by foreign material, necrosis of the liver, cholemic nephrosis, bilateral bronchopneumonia, and atherosclerosis of the aorta.

CASE 2. A.S., a 34 year old white woman, was admitted to the Hospital of the University of Pennsylvania on April 27, 1924, on the surgical service of Dr. George P. Muller. Cholecystostomy had been performed in 1922 at another hospital and over 200 gallstones removed. The wound drained for 3 months after operation. On April 21, 1924 she developed right upper quadrant pain and vomited bile stained fluid. By April 24, fever and abdominal pain and tenderness were present. On admission the patient had no tenderness at the scar of the previous cholecystostomy but had a large, firm, tender mass in the left upper quadrant. The leucocyte count was 9,500 per cubic millimeter. Dr. Muller made a diagnosis of hydrops of the gall bladder and on April 29, 1924, explored the abdomen. The omentum was attached to the anterior abdominal wall and to the liver. In separating these structures, the operator entered a lemon sized mass that extended into the region of the gall bladder. Vigorous bleeding ensued immediately and could not be controlled by ligation or hemostats. The area was packed tightly with gauze and the wound closed. A diagnosis of aneurysm of the hepatic artery was made at operation.

Postoperatively there was constant oozing from the wound until the fourth day, when sudden hemorrhage of about a pint of blood necessitated repacking of the wound. Two days later the wound was explored in the operating room. When the packing was removed, severe bleeding compelled the operator to repack without further exploration. Oozing from the wound continued, and on the ninth postoperative day another severe hemorrhage caused the patient's death. Postoperative examination through the wound showed a large sac into which the hepatic artery opened near its origin from the celiac axis. Autopsy permission was not granted.

DISCUSSION

General. Although an aneurysm had not been suspected in these 2 patients, the surgeon recognized the lesion during operation. We were able to find reports of 14 patients with hepatic aneurysm who had been operated on for symptoms or signs of the aneurysm; in only 9 was the aneurysm recognized at the laparotomy (1, 3, 6, 10, 11, 14, 20, 21, 33). The great majority of aneurysms have been recognized only at the autopsy table. In operating on patients with biliary tract disease, the surgeon must be alert for signs of aneurysm in order to apply quick and effective treatment.

According to recent summaries (23, 25) the development of hepatic aneurysm is related to infection in about 60 per cent of instances. Arteriosclerosis and trauma account for the next largest groups. Traumatic aneurysms have usually been intrahepatic. The other types have usually been extrahepatic and have caused pain (80 per cent), hemorrhage from the gastrointestinal tract (63 per cent), jaundice (55 per cent), and more rarely liver enlargement, a pulsating tumor, a palpable thrill, and a systolic bruit. The average age of the patients was 38 years; and the disease occurred three times as often in males as in females. Aneurysms commonly increase in size until they rupture, although in 3 instances they were found intact at autopsy (15, 22, 26). When they erode into the biliary or gastrointestinal tract, hematemesis or melena ensues. When aneurysms perforate into the peritoneal cavity, death from massive hemorrhage is immediate.

If the patient is seen at an early stage when the aneurysm is still small but eroding into the biliary ducts, his presenting complaint will be hematemesis or melena, and obstruction of the hepatic or common ducts will probably have produced jaundice. In the presence of pain, bleeding from the gastrointestinal tract, and jaundice, the diagnosis of aneurysm of the hepatic artery is not unlikely. It may be considered almost certain if, also, a pulsating mass is felt or a systolic bruit is heard.

Ligation of the hepatic artery. The 3 recorded cures of aneurysm of the hepatic artery were all obtained by ligation of the artery.[1] Kehr

[1]Anderson's case, reported by some as a cure of aneurysm by ligation, should not be included because the site of aneurysm and the site of suture were not determined.

in 1903 operated on a patient with an aneurysm of the right branch of the hepatic artery, and obtained a cure by ligating the artery distal to the point of origin of the gastroduodenal artery. Kading reported that Sudeck in 1915 ligated the artery proximal to all its branches and cured a patient with an intrahepatic aneurysm that developed after a penetrating gunshot wound of the liver. Colmers in 1921 reported the cure of an intrahepatic aneurysm resulting from injury by the ligation of the common hepatic artery. Many authors have objected to ligation of the artery because of the frequency of death from liver necrosis (11, 12). If, however, the artery is ligated proximal to its larger branches—the right gastric and the gastroduodenal arteries—circulation can continue via anastomoses with the left gastric and superior mesenteric arteries (21, 33). If the lumen of the artery is narrowed by disease, as usually takes place with aneurysm, anastomoses may develop with the inferior phrenic arteries, and ligation of the hepatic distal to the gastroduodenal may be successful. Accessory hepatic arteries arising from other branches of the aorta have been reported in as high as 46 per cent of cadavers and may supply sufficient collateral circulation (5). Finally, experimental work in dogs (17) shows that while sudden ligation of healthy hepatic arteries just proximal to their bifurcation is uniformly fatal, multiple stage ligations of the artery, beginning proximally and proceeding distally, are safe.

The recent experiments of Markowitz and associates have provided information that may be of value in preventing death following ligation of the hepatic artery in humans. While studying the effect of anastomoses between the hepatic artery and portal vein in dogs, these investigators noted that dogs given parenteral doses of penicillin did not die following ligation of the hepatic artery. This observation was confirmed in our laboratory and other antibiotics were tested (8). Aureomycin given parenterally was just as effective as penicillin in preventing death after ligation of the dog's hepatic artery and its branches. Dogs untreated by antibiotics usually died within 48 hours of ligation with peritonitis and massive hepatic necrosis, but dogs receiving parenteral penicillin or parenteral aureomycin for 5 days following ligation lived in moderately good condition until sacrificed at 21 days. At autopsy no hepatic necrosis was observed. No peritonitis was noted in the dogs treated with aureomycin, and only a mild peritonitis in those treated with penicillin. Streptomycin, given parenterally to a small number of dogs, has prolonged the length of life in all instances although it has prevented death in only a third.

We believe that these observations may be of great importance to the clinician, and that massive doses of the antibiotics may prevent death in humans following ligation or thrombosis of the hepatic artery. Although our first patient had both penicillin and streptomycin in large doses, two special factors may have caused an unusual degree of hepatic anoxia and, therefore, liver necrosis: first, the large gauze packs may have partially blocked the portal blood flow; and second, the patient had a long period of hypotension before and during the second operation.

Reconstruction of the hepatic artery. Successful reconstruction of the hepatic artery after excision of an aneurysm has never been recorded. Gordon-Taylor described aneurysmorrhaphy with closure of the aneurysm in layers so as to maintain the patency of the arterial lumen, but the patient died 40 hours after operation. In recent years defects in many arteries have been successfully bridged by arterial and vein grafts (4, 7, 13, 18, 30). In experimental animals defects in arteries of only 5.0 millimeters in diameter have been successfully repaired by venous grafts (19). Similar procedures might be feasible in the human hepatic artery, especially if the aneurysm were well proximal to the hilum of the liver. Another solution might be to excise the aneurysm and anastomose its distal end to a contiguous artery that could safely be sacrificed; viz., gastroduodenal, right gastric, splenic. Limiting factors in the success of these reconstructive operations include: (1) the difficulty of obtaining the necessary exposure because of adhesions and surrounding vital structures; (2) the long operating time, during which the liver would be deprived of its ar-

terial blood; (3) the small size of the vessels involved; and (4) the danger of subsequent thrombosis.

The recent experiments of Fine and associates (9) on hemorrhagic shock in dogs have shown that perfusion of the liver with well oxygenated blood would preserve the integrity of this organ although the remainder of the animal were exposed to a state of shock that otherwise would result in irreversibility. While the liver is being deprived of its arterial blood during the extensive operations here described, the perfusion of well oxygenated blood through a portal tributary might prevent liver anoxia.

Excision of the aneurysm and insertion of a prosthetic tube of nonirritating material, viz. lucite (16), might be justified, although thrombosis is more likely to occur than with grafts of artery or vein. If the anastomosis remained patent for only a short time, however, irreversible changes in the liver might be prevented. The balance between liver competency and incompetency following ligation is narrow, and a few hours of hepatic arterial supply might allow enough collateral circulation to develop to prevent liver necrosis, especially if large doses of the antibiotics were given.

Other surgical approaches. An easier operation than grafting and one that has been reported to be successful in animals (27, 32) is anastomosis of the proximal end of the divided hepatic artery, or one of its branches, to the portal venous system. By this means the arterial supply to the liver may be maintained after division of the artery and liver anoxia prevented. As far as we can determine, this operation has not been attempted in the human.

Another therapeutic approach consists in wrapping cellophane, polythene, or similar plastic material about the aneurysm or about the artery proximal to the aneurysm. The fibrosis secondary to cellophane implantation has been reported to be successful in obliterating aneurysms and occluding blood vessels (28, 29, 35). The type of material that produces the greatest fibrosis is a matter of considerable dispute. Some investigators have expressed the opinion that dicetyl phosphate, an adulterant of polythene film, is the active tissue excitant. Work in our laboratory on the production of coronary artery narrowing in dogs (31) indicates that MT-31 cellophane (containing a moisture proofing agent) is more effective in producing fibrosis and narrowing than pure polythene or polythene with dicetyl phosphate. We postulate that the moisture proofing agent may be the active ingredient. Until uniform results can be obtained with the same material, it would seem best not to use this method clinically except as a last resort.

SUMMARY

1. Aneurysm of the hepatic artery, although a rare cause of biliary symptoms, must be considered in the differential diagnosis of jaundice. Hepatic aneurysm produces pain, jaundice, and bleeding into the gastrointestinal tract. Heretofore, the diagnosis has rarely been made before death and only 14 patients with aneurysm have been operated on.

2. Two additional hepatic aneurysms, both diagnosed at operation, are reported. Both patients died—one from massive hepatic necrosis, the other from recurrent hemorrhage.

3. The only reported cures of hepatic aneurysm have been achieved by ligation of the artery. Several recent developments may improve the results of treatment, although to our knowledge they are still untested in humans: (1) the use of antibiotics in the prevention of liver necrosis following ligation; (2) reconstruction of the artery by grafts of artery or vein; and (3) anastomosis of the ligated hepatic artery to the portal system.

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SAPHENOFEMORAL JUNCTION ANOMALIES

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HIGH saphenous ligation is probably performed as frequently as any other single operative procedure. Misunderstanding of the operative procedure seems to be widespread and apparently stems from a lack of knowledge of normal and anomalous anatomy of the venous patterns in and about the fossa ovalis. In this clinic, 4 cases of recurrent saphenous varicosities recently have had secondary operations. Except for an old scar, exploration of the saphenofemoral area failed to reveal evidence of previous ligation of the saphenous vein. In 1 case, three black silk ligatures were found, apparently having been used to ligate each of three small venous tributaries. The great saphenous vein and an equally large lateral accessory saphenous were intact. The original incision in these cases was parallel with the inguinal ligament.

The usual description of saphenous vein anatomy at the saphenofemoral junction is as follows (3): "In its course through the thigh it communicates through the deep fascia with the deep veins, and it receives the following tributaries: (1) The lateral femoral circumflex vein, from the anterior and lateral parts of the thigh. (2) The medial femoral circumflex vein, which commences at the back of the knee where it frequently communicates with the small saphenous vein. The medial femoral circumflex vein runs upwards, curves round the medial side of the thigh and joins the great saphenous vein midway between the hip and the knee." [In this study, we refer to the lateral and medial femoral circumflex veins as the lateral and medial femoral cutaneous veins.] "(3) The external superficial pudendal vein. (4) The superficial epigastric vein, and (5) the superficial circumflex vein. The last three tributaries join the great saphenous vein just before it passes through the fossa ovalis."

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In an attempt to clarify the problem, we have reviewed the results of some 650 dissections of the saphena magna at the fossa ovalis and have recorded additional dissections from this clinic. Anomalies which occur in and around the fossa ovalis will be discussed and classified, as well as the usual incision for surgical approach.

Daseler and associates, in an extensive study of 550 dissections of the fossa ovalis, divided the anomalies into 8 types. Glasser, in 100 dissections, separated the anomalous venous patterns at the saphenofemoral junction into 19 separate categories. A composite study of the problem reveals that certain general classifications can be made. Anomalies listed by Daseler and Glasser, as well as ours, can be grouped as follows:

1. One or all of the superior tributaries may fuse before terminating in the saphenous or femoral veins. It is impractical for the surgeon to remember in detail all of the variations that may occur. We feel that it is sufficient to remember that tributaries may fuse.

2. One or all of the superior tributaries may empty directly into the femoral vein. Obviously, these anomalies are not important with reference to saphenous varicosities.

3. One or all of the superior tributaries may drain into a medial or lateral accessory saphenous vein.

4. One or all of the superior tributaries may join a medial or lateral femoral cutaneous vein.

5. Several rare anomalies should be noted which do not fall into any general grouping:

a. Lateral femoral cutaneous, saphena magna and accessory saphenous may all be present and of approximately equal caliber.

b. The saphena magna may pierce the deep fascia of the thigh to enter the femoral vein approximately 1 inch below the fossa ovalis.

c. A lateral femoral cutaneous vein may drain directly into the femoral vein above the fossa ovalis.

Remembering then, that fusion of tributaries may occur, that any or all of the tributaries may empty directly into the femoral vein, and that the listed rare anomalies may be present, we have narrowed the classification of high saphenous anomalies into three groups. This proposed classification will be discussed later.

INVESTIGATIONAL PROCEDURE

Sixty-one saphenous dissections were done either on fresh autopsy material or in our ligation clinic. Thirty-seven were done through a vertical incision, and 24 through a transverse incision parallel with Poupart's ligament. The initial length of each incision was 6 centimeters. All branches emptying into the superior reaches of the saphenofemoral bulb were dissected up to the inguinal ligament. All other tributaries were dissected for a distance of at least 3 centimeters. The greater saphenous, and when present, an accessory saphenous, in each instance, was dissected distally for a distance of 6 centimeters. (This procedure necessitated elongation of the original incision.) All femoral cutaneous veins were dissected distally within the limitations of the incision. The incision, regardless of type—vertical or horizontal—passed through a constant predetermined point, that site being selected as the surface anatomical landmark of the fossa ovalis. This point was arbitarily selected as being 3 centimeters lateral to the pubic tubercle, and 3 centimeters below the inguinal ligament, or for practical purposes, two finger breadths lateral and two finger breadths below the above named points (Fig. 1).

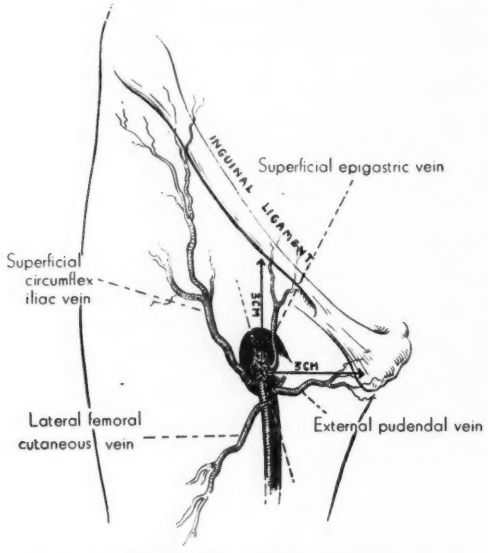


Fig. 1. Use of 3 centimeter rule in locating the saphenofemoral junction. Dotted line passing over the fossa ovalis is the incision preferred by the authors.

INVESTIGATIONAL DATA

Using the above method, the saphenofemoral junction was not accurately located in 3 cases, or 5 per cent of the total. Each of these errors in location of the fossa ovalis occurred in obese individuals, and in each instance the fossa was found above the predetermined point. In obese patients, the pubic tubercle and Poupart's ligament are less easily palpated. In addition, the overlying structures tend to be more mobile and redundant, making determination of the saphenofemoral bulb more difficult (Table I).

Anomalies found in our dissections have been divided, for purposes of simplicity, into three categories:

Group I. One or more superior major tributaries empty into a medial or lateral accessory saphenous (Table II).

Group II. One or more tributaries empty into a medial or lateral femoral cutaneous vein (Table II).

Group III. More than three superior tributaries may be found emptying into the saphenofemoral bulb. Ten such specimens were found, an incidence of 16.4 per cent (Table II). This type is included since it has been noted that occasionally some surgeons satisfy themselves with ligation of the first three tributaries which they uncover, and then ligate the greater saphenous without adequately cleaning the fat pad from the sapheno-

TABLE I.—THREE CENTIMETER RULE IN DETERMINING SITE OF FOSSA OVALIS

	No.	Per cent
Total number of dissections	61	100
Within 1 cm. of fossa	58	95
Not within 1 cm. of fossa	3	5

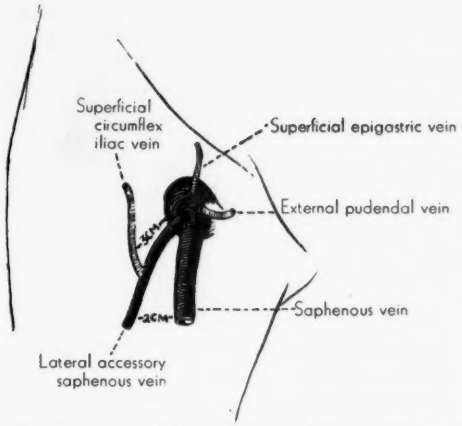
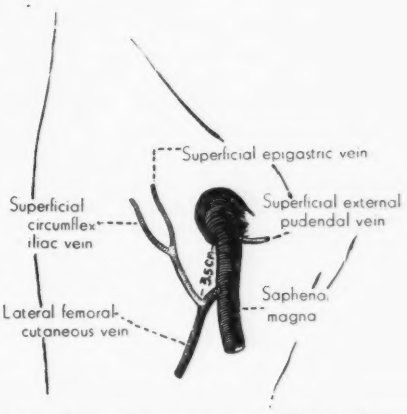


Fig. 2. Type 1. Major tributary emptying into lateral accessory saphenous vein. The incidence of major tributaries draining into a medial or lateral accessory saphenous vein is 13.1 per cent.



Type 2. Major tributary emptying into lateral femoral cutaneous vein. The incidence of major tributaries draining into a medial or lateral femoral cutaneous vein is 9.8 per cent.

femoral junction and the tributaries which remain in that area. Many times, additional branches at the femoral bulb can be found ending in large lymph nodes in the immediate vicinity of the fossa ovalis.

Fifteen accessory saphenous veins were noted—an occurrence of 24.6 per cent. Tributaries emptying into an accessory saphenous were noted 8 times, or an incidence of 13.1 per cent. Major tributaries were found to empty into a medial or lateral femoral cutaneous vein in 6 cases, an incidence of 9.8 per cent. Typical examples of these anomalies can be found in Figures 2 and 3.

In many cases, the major tributaries (superior epigastric, superficial circumflex iliac and superficial external pudendal) entered an accessory saphenous or a medial or lateral femoral cutaneous vein at a distance of 3 to 3.5 centimeters below the lower border of the fossa ovalis. None were found to empty at a distance greater than 3.5 centimeters. If the fatty and areolar tissue is not removed for at least this distance, these anomalies will be missed.

We believe that all tributaries emptying into the saphenofemoral junction should be dissected for a distance of 3.5 centimeters from the site of entry. Branches emptying into the

TABLE II.—INCIDENCE OF THREE MAJOR TYPES OF ANOMALIES

	No.	Per cent
Tributaries emptying into accessory saphenous	8	13.1
Tributaries emptying into medial or lateral femoral cutaneous	6	9.8
More than 3 tributaries emptying into femoral bulb	10	16.4
Combination of I and III	4	6.5
Combination of II and III	2	3.3
Total incidence of all kinds	18	29.0

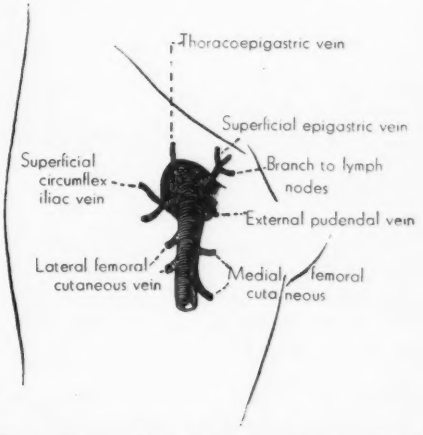


Fig. 3. Type 3. More than three tributaries emptying into the saphenous or saphenofemoral junction, exclusive of the femoral cutaneous and accessory saphenous veins. Incidence, 16.4 per cent.

bulb may serve as masks for anomalies occurring more distally.

Anomalies, in our experience, were much more difficult to demonstrate through the parallel or transverse incision. This incision, sometimes requires extensive undermining in order to expose anomalous structures. Comparative observations of the two incisions have led us to believe that the longitudinal one is superior for the following reasons:

1. The longitudinal incision is made over the approximate course of the major saphenous vein and thereby affords better exposure for a greater distance.

2. Extensive undermining is not necessary for exposure of anomalous tributaries.

3. The incision can be extended distally or proximally with ease and the degree of exposure thus afforded is comparatively greater.

The incision which we prefer begins 1 centimeter below Poupart's ligament, extending downward and slightly medially for a distance of 8 to 9 centimeters (Fig. 1). An incision 6 centimeters in length is not considered adequate.

SUGGESTED TECHNICAL MANAGEMENT

The following outlined procedure is suggested as a possible means of increasing the efficacy of high saphenous ligation, and minimizing the possibility of overlooking anomalies:

1. Accurate location of the saphenofemoral junction.

2. Longitudinal incision 8 to 9 centimeters in length, as described, passing through the predetermined location of the fossa ovalis.

3. Incision of the superficial fascia and exposure of the saphenous vein by either blunt or finger dissection.

4. Dissection of the saphenous vein from the lowest point of exposure to the saphenofemoral junction with removal of the fat pad.

5. Dissection of saphenous tributaries in all directions for a distance of at least 3.5 centimeters.

6. Ligation and excision of exposed portion of the saphena magna and all tributaries.

Removal of the fat pad can be accomplished with comparative ease by exposing the saphenous vein by finger dissection, and dissecting off the fatty tissue by blunt dissection. Using this method, small tributaries will occasionally be found draining directly into the anterior surface of the saphenous vein. However, the caliber of these vessels is small, and if torn, bleeding is minimal and easily controlled. In no instance did we find a major tributary emptying into the anterior surface of the saphena magna either along its course or at its junction with the femoral vein.

It should be borne in mind that when ligating the saphenous and its tributaries at their junction with the femoral vein, excessive pull on the saphenous may drag the femoral vein superficially and through the fossa ovalis. Thus it may be narrowed or ligated inadvertently. Varicose veins are thin walled and extremely fragile, and, if subjected to excessive pull, will tear easily. In the region of the fossa such a tear may involve the femoral vein with consequent difficult bleeding.

SUMMARY

1. The results of 61 saphenofemoral junction dissections are recorded and analyzed, in addition to other previously recorded series.

2. Anomalies which occur at the saphenofemoral junction are briefly and simply classified.

3. The usual types of incision for high saphenous ligation are contrasted.

4. A procedure of technical management as a possible means of increasing the efficacy of high saphenous ligation is offered.

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SURGICAL SCRUBBING WITH *p*HISODERM G-11 AS APPLIED TO A MATERNITY HOSPITAL

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THE aseptic techniques used in a maternity hospital must be under constant surveillance if proper protection is to be given the parturient and her infant. Puerperal sepsis is still the most frequent cause of maternal death. Furthermore, the epidemic character of infantile diarrhea is an additional hazard of which a maternity unit must be aware. Certain organisms of the former may not be effectively treated by antibiotics, while in the latter instance both the etiological agent and the mode of transmission of the disease are unknown. These facts are often forgotten in this age of effective chemotherapeusis.

The need to perform a delivery without adequate preparation of the hands is a constant threat to a break in technique. The lying-in care of many patients taxes the surgical conscience of the nurse with respect to hand care because of her desire to save time. Hence, any new technique which is safe bacteriologically, which will save scrubbing time and which will not produce trauma to the skin of the hands would appear desirable.

A previous communication as part of this study presented data consistent with the conclusion that there are certain advantages for using the detergent *p*Hisoderm G-11[1] rather than the routine soap scrub as it applies to nursery care (1). It is the purpose of this paper to report on bacteriological and clinical experience with the use of *p*Hisoderm G-11 for the preparation of the hands and arms as part of the aseptic technique necessary for deliveries and other operative procedures which occur in obstetrical practice.

Experimental work on the effectiveness of G-11 has been reported by a number of investigators. Traub (7) found by incorporating 2 per cent G-11 in cake soap he was able to reduce the resident bacterial flora of the hands and forearms to a remarkably low count. He (8) also carried out comparative tests using a toilet soap as control. From these experiments he concluded that by using G-11 soap regularly, the individual has a lower resident bacterial count after 2 minutes' washing than an individual who washes with ordinary toilet soap for 20 minutes. He further pointed out that if the maximum benefit from G-11 soap is to be obtained for surgical scrubs it must be used exclusive of all other soaps, because a period of contact with the material induces a cumulative bacteriostatic action.

More recent experiments by Seastone substantiate the remarkable effectiveness of G-11 as an antibacterial agent in maintaining surgical cleanliness of the hands and forearms. He incorporated 1 per cent G-11 in a liquid soap in order to obtain a more uniform application of G-11 to the skin than he found possible with a bar soap. He suggested a surgical scrub procedure which required 6 minutes' exposure time to the 1 per cent G-11 soap solution with a 5 second rinse in 1:1000 aqueous

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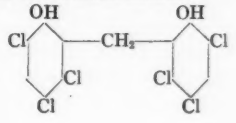
[1]The antibacterial agent reported in this study consists of a synthetic detergent *p*Hisoderm fortified with 3 per cent hexachlorophene or G-11. It will be referred to hereafter as *p*Hisoderm G-11. *p*Hisoderm is a mixture of sodium octylphenoxyethoxyethyl ether sulfonate, lanolin cholesterols, and petrolatum. Its consistency is that of a thick creamy fluid. It has a *p*H of 5.5 approximating that of average normal skin. It contains no alkalis and does not hydrolyze to form sulfuric acid. *p*Hisoderm lowers the surface tension of water and is an active emulsifying agent. These attributes make it about 40 per cent more active than regular soap as a cleansing agent (2). Skin sensitivity tests carried out by Guild are reported negative. G-11 or hexachlorophene has the following chemical composition 2,2′ dihydroxy, 3,5,6, 3′,5′,6′ hexachlorodiphenylmethane. Its structural formula is



zephiran. He explained that the rinse was used to destroy "hypothetical organisms present in the tap water left on the hands." If a fresh sterile water rinse were available the zephiran rinse might be omitted. He found that after the routine use of the above scrub for a period of 5 days followed by a 2 day lapse the persistent effectiveness of G-11 could still be demonstrated. From this he concluded that it was unnecessary for the surgical team to be subjected daily to contact with the agent to maintain its effectiveness unless a lapse of more than 2 days occurred. He also pointed out that with the maintenance of a high level of the agent on the skin, a brief wash with G-11 soap between glove changes would prevent the rise in bacterial numbers which occurred with ordinary procedures. Fahlberg, Swan, and Seastone demonstrated the retention of hexachlorophene (G-11) on the skin and the persistence of its bactericidal effect.

Hufnagel, Walter and Howard compared the effectiveness of various detergents and antibacterial agents by using a mechanical device which produced a standardized scrub. Bacterial determinations made from these identical scrubs using coconut oil soap, plain *p*Hisoderm and *p*Hisoderm with 3 per cent G-11 indicated that the latter combination produced the most rapid disinfecting action. An additional finding showed that *p*Hisoderm without G-11 possessed a cleansing action equal to that of other detergents tested.

The study being reported was designed to determine the effectiveness of *p*Hisoderm G-11 as a surgical scrub in a maternity hospital. In addition, its value in reducing scrubbing time was investigated. Bacteriological data are presented in the following order:

1. Bacterial counts from the skin of the hands: (a) before and after *p*Hisoderm G-11 scrub, (b) following *p*Hisoderm G-11 scrub in contrast to soap scrub.

2. The persistence of the antibacterial effect of *p*Hisoderm G-11.

3. The possibility of "trapping" bacteria beneath a film of G-11 formed by the routine use of *p*Hisoderm G-11.

4. The advantages and limitations of *p*Hisoderm G-11 especially as it applies to a reduction in scrubbing time.

MATERIALS AND PROCEDURES

The subjects for this study were medical students, surgical nurses, members of the house and visiting staffs of the Boston Lying-in Hospital and surgical nurses at the Free Hospital for Women. The first experiment was directed toward determining the effectiveness of *p*Hisoderm G-11 as a cleansing agent. Medical students were used as subjects and the following procedure was carried out:

Sterile surgical gloves were placed on untreated hands immediately after arrival of the subjects in the laboratory. One hour later the gloves were carefully removed without reversal, and each glove was filled with 100 cubic centimeters of sterile distilled water. Each glove was massaged 25 times, and a 1 cubic centimeter sample was removed and plated in tryptic digest agar[1] reinforced with sterile horse serum to determine colony counts for the estimation of the number of bacteria per cubic centimeter of rinse water. This is referred to as the "control count."

Immediately after removal of the gloves for sampling, each subject carried out the following "scrub" procedure, using *p*Hisoderm G-11.

1. The hands were wetted to a line 5 centimeters above the wrist. About 3 cubic centimeters of *p*Hisoderm G-11 was rubbed over each hand. The brush was moistened and the hands were then thoroughly scrubbed, 30 strokes for the skin and 50 strokes for the nails of each hand. The scrub consumed approximately 10 minutes.

2. The hands were then thoroughly rinsed with tap water and air dried. Each subject put on a fresh set of sterile rubber gloves as soon as the hands were sufficiently dry. Four hours after the scrub, gloves were removed and cultured as described above. The subjects continued with their normal duties while wearing the gloves. The bacterial counts are reported as the number of bacteria per 1 milliliter of wash water from the gloves.

The same procedure was used in a group of surgical nurses to compare the effectiveness of the routine surgical soap scrub with the *p*Hisoderm G-11 scrub.

[1]Tryptic digest media consists of beef heart digested by Pfanstiehl trypsin prepared in the media room of the Department of Bacteriology, Harvard Medical School.

To investigate the persistence of the antibacterial effect of *p*Hisoderm G-11 on the resident flora of the skin the following experiments were undertaken. A subject using the same routine as outlined scrubbed daily with *p*Hisoderm G-11 for 3 successive days. A lapse of 2 days occurred after which scrubbing with *p*Hisoderm G-11 was resumed on the sixth and seventh days. *p*Hisoderm G-11 scrubs were again omitted until the fourteenth day. Bacterial counts were recorded following each scrub.

The persistence of the antibacterial effect of *p*Hisoderm G-11 was again compared to that of soap in the following manner. Without previous skin preparation and with the use of a sterile nylon bristle tooth brush, a 90 second soap scrub was carried out over a circumscribed area of 4 centimeters on the palmar surface of the left hand. The same individual repeated this procedure on alternate days for 11 days. Cultures were taken by rinsing the brush in 10 cubic centimeters of sterile broth to which 20 cubic centimeters of melted cooled agar was added and pour plates were made. These were incubated at 37 degrees C. for 48 hours when the colonies were counted. After an interval of 5 days free from surgical scrubbing, a second series of observations was made on the same individual substituting *p*Hisoderm G-11 for soap. The technique and methods of culture were the same as those already described.

In order to investigate the problem of "trapping" bacteria beneath a film produced by the routine use of *p*Hisoderm G-11, the following procedure was adopted. Six subjects were instructed to use *p*Hisoderm G-11 exclusively for a period of 5 days. At the end of this period, a circumscribed area approximating 4 centimeters on the palmar surface of the left hand was scrubbed for 90 seconds first with a cotton applicator moistened with sterile broth and cultured as in the previous experiment. Following this, a vigorous scrub with a sterile nylon bristle tooth brush moistened with sterile broth was carried out and cultures again were taken.

The next 2 experiments were carried out to ascertain whether the continued use of this detergent would allow for a reduction in the scrubbing time, in other words to determine the conditions under which a maximum antibacterial effect of *p*Hisoderm G-11 might be obtained.

TABLE I.

	Bacterial counts from gloves worn for 1 hour on unscrubbed hands*		Bacterial counts from gloves worn for 4 hours after scrub with *p*Hisoderm and 3 per cent G-11*	
No.	Right	Left	Right	Left
1	57	41	3	14
2	110	100	3	3
3	371	61	2	3
4	42	101	43	4
5	1702	410	18	13
6	20	94	2	8
7	107	154	0	1
8	11	13	3	11
9	31	106	0	1
10	85	100	0	0
11	82	47	1	0
12	42	27	0	0
13	176	34	0	0
14	860	580	59	0
15	1192	1100	2	3
16	830	710	4	12
17	3	41	0	0
18	52	53	0	0
19	6	11	5	9
20	328	152	17	25
21	116	55	4	5
22	1800	2500	3	1
23	10	3	3	0
24	12	15	0	0
25	3	4	0	2
26	30	20	2	0
27	768	385	0	1
28	15	54	1	1
29	1528	2712	4	6
30	127	22	1	0
Totals	10576	9708	182	123
Averages	332.3	323.5	6.0	4.1

*Bacteria in 1 c.c. of wash water, multiply by 100 to get the total count from each glove.

Bacterial counts were made of the gloves worn by two groups of personnel. One group was composed of residents, internes, and nurses who scrubbed daily, while members of the visiting staff who did not scrub every day

TABLE II.—BACTERIAL COUNTS ON GLOVES WORN BY SURGICAL NURSES FOLLOWING 10 MINUTE SCRUBS

Group A—10 minute conventional soap scrub*			Group B—10 minute scrub with *p*Hisoderm and 3 per cent G-11*		
No.	Right glove	Left glove	No.	Right glove	Left glove
1	0	6	1	1	11
2	0	0	2	2	2
3	11	14	3	0	0
4	1	0	4	0	1
5	30	0	5	0	0
6	0	0	6	3	1
7	100	30	7	3	0
8	2	1	8	3	0
9	2	3	9	2	1
10	2	47	10	0	0
11	8	11	11	0	2
12	0	3	12	6	12
13	0	4	13	2	2
14	1	0	14	2	1
15	20	24	15	0	1
16	3	0	16	6	3
17	13	4	17	0	0
18	0	0	18	2	0
19	259	385	19	0	2
20	1	0	20	2	0
21	2	0	21	1	0
22	31	28	22	4	2
23	2	2	23	0	1
24	0	1	24	0	0
25	0	2	25	0	0
26	0	0	26	0	1
27	0	1	27	2	1
28	0	0	28	13	1
Totals	488	566		54	45
Averages	17.4	20.2		1.9	1.6

*Bacteria in 1 c.c. of wash water, multiply by 100 to get the total count from each glove.

made up the second group. Records were kept including the length of time of each individual scrub; and whenever possible, the time lapse since the last contact with *p*Hisoderm G-11.

A study of the "90 second" scrub was carried out by medical students on delivery service. Each student was instructed to perform the 10 minute scrub with *p*Hisoderm G-11 for

TABLE III.—REPEATED BACTERIAL COUNTS ON THE SAME SUBJECT

Day	Control count Gloves worn 1 hour*		After *p*Hisoderm G-11 scrub Gloves worn 3 hours*	
	Right glove	Left glove	Right glove	Left glove
1st	3830	1380	10	0
2nd	320	140	0	0
3rd	10	30	60	0
4th	omitted	omitted	omitted	omitted
5th	omitted	omitted	omitted	omitted
6th	91	86	8	20
7th	15	13	6	0
(6 days)	omitted	omitted	omitted	omitted
14th	112	101	3	10

*Bacteria in 1 c.c. of wash water, multiply by 100 to get the total count for each glove.

the first 3 days on service. He then substituted a 90 second scrub with *p*Hisoderm G-11 whenever he assisted in any obstetrical procedure. Sterile rubber gloves were worn one hour following a 90 second scrub, and from these gloves cultures were taken as described previously.

The scrub procedure using *p*Hisoderm G-11 and a nylon bristle brush is briefly described as follows:

Those individuals who scrub:

a. At intervals of 3 days or longer use 30 brush strokes to each skin area, 50 strokes to the finger nails, which requires approximately 10 minutes.

b. At intervals of 2 days use 15 brush strokes to each skin area, 25 strokes to the finger nails, which requires approximately 5 minutes.

c. Daily and use *p*Hisoderm G-11 for routine hand wash, use 9 strokes to each skin area, 15 to the finger nails, which requires approximately 90 seconds and has been referred to as the "90 second" scrub.

In any experiment involving a bactericidal agent, there is always the possibility of a small amount of the material being transferred to the culture medium. To obviate this source of error, serum was added to the media as suggested by Seastone who noted that the bacteriostatic potency of G-11 was reduced by the addition of 1 per cent sterile serum to the broth or agar cultures.

TABLE IV.—TOTAL NUMBER OF BACTERIA IN THE 4 CENTIMETERS CIRCUMSCRIBED AREA OF PALM OF HAND

Series A After 90 second scrub with soap		Series B After 90 second scrub with *p*hisoderm G-11	
Day	Count	Day	Count
1st	508	16th	320
3rd	1002	18th	49
5th	748	20th	324
7th	1408	22nd	12
9th	968	24th	22
11th	2184	26th	6

TABLE V.—TOTAL NUMBER OF BACTERIA IN THE 4 CENTIMETERS CIRCUMSCRIBED AREA OF PALM OF HAND

Subjects	Series A 90 second scrub with cotton applicator	Series B 90 second scrub with nylon bristle brush
1	8	0
2	0	0
3	8	0
4	2	6
5	0	8
6	0	0

RESULTS

The results of the first experiment as shown in Table I reveal that a *p*Hisoderm G-11 scrub reduces the bacterial counts of the hands to an almost negligible number. In 20 out of 30 medical students used in this study, bacterial counts from gloves worn following the *p*Hisoderm G-11 scrub were reduced to 5 or less per 1 cubic centimeter of wash water in both the right and left hands.

In Table II bacterial counts following a 10 minute scrub with *p*Hisoderm G-11 are compared with those following a similar scrub with tincture of green soap. Of the 28 subjects on *p*Hisoderm G-11 there were no marked elevations in bacterial counts at any time; whereas, elevations did occur in a few instances following the soap scrub.

The data in Table III indicate the persistence of the antibacterial effect of *p*Hisoderm G-11. There is evidence of a cumulative effect also, since the control counts become progressively lower on each successive day fol-

TABLE VI.—BACTERIAL COUNTS ON GLOVES WORN BY RESIDENT HOUSE STAFF FOLLOWING *p*HISODERM G-11 SCRUB.* LENGTH OF SCRUB IS RECORDED.

Number	Length of scrub in minutes	Gloves		Number	Length of scrub in minutes	Gloves	
		Right	Left			Right	Left
1	11	624	564	42	10	0	0
2	11	1	1	43	10	1	0
3	12	1	0	44	10	1	8
4	10	24	†	45	10	3	0
5	10	194	11	46	10	0	0
6	10	23	0	47	10	3	0
7	10	78	12	48	10	2	0
8	10	0	0	49	8	1	1
9	10	0	1	50	8	14	6
10	10	4	2	51	8	8	2
11	10	0	0	52	8	10	10
12	10	10	10	53	8	0	0
13	10	10	0	54	8	0	0
14	10	0	†	55	8	0	0
15	10	1	†	56	8	4	1
16	10	0	0	57	7	4	1
17	10	27	4	58	6	2	0
18	10	5	3	59	6	2	0
19	10	0	0	60	6	0	1
20	10	3	1	61	5	1	1
21	10	3	30	62	5	—	3
22	10	0	1	63	5	9	7
23	10	0	0	64	5	1	0
24	10	0	0	65	5	2	—
25	10	2	12	66	5	5	30
26	10	0	1	67	4	2	3
27	10	1	1	68	4	2	13
28	10	0	†	69	3	21	7
29	10	0	0	70	3	0	0
30	10	0	3	71	3	1	0
31	10	0	0	72	3	0	1
32	10	0	0	73	3	2	0
33	10	2	0	74	3	0	1
34	10	4	7	75	3	0	0
35	10	2	1	76	3	1	0
36	10	1	1	77	3	1	0
37	10	0	0	78	3	0	0
38	10	5	2	79	3	5	1
39	10	5	3	80	3	1	0
40	10	2	1	81	3	2	0
41	10	0	0	82	3	0	0

*Bacteria in 1 c.c. of wash water, multiply by 100 to get the total count from each glove.
†Glove missing.

TABLE VII.—BACTERIAL COUNTS ON GLOVES WORN BY THE SURGICAL NURSING STAFF FOLLOWING *p*HISODERM G-11 SCRUB.* LENGTH OF SCRUB IS RECORDED

Number	Length of scrub in minutes	Gloves		Number	Length of scrub in minutes	Gloves	
		Right	Left			Right	Left
1	10	0	1	23	10	79	20
2	10	1	3	24	8	2	4
3	10	5	2	25	8	—	3
4	10	4	†	26	8	—	2
5	10	†	0	27	8	4	3
6	10	†	75	28	8	0	3
7	10	0	0	29	8	1	0
8	10	0	0	30	8	0	3
9	10	1	0	31	8	0	0
10	10	1	0	32	8	1	2
11	10	1	30	33	8	4	1
12	10	20	10	34	7	5	0
13	10	11	1	35	7	0	1
14	10	4	2	36	6	2	0
15	10	180	4	37	6	—	0
16	10	†	0	38	6	0	0
17	10	0	0	39	5	—	10
18	10	0	0	40	5	3	1
19	10	1	0	41	5	4	7
20	10	0	0	42	2	1	0
21	10	0	0	43	2	2	1
22	10	†	83	44	2	1	2

*Bacteria in 1 c.c. of wash water, multiply by 100 to get the total count from each glove.
†Glove missing.

lowing a *p*Hisoderm G-11 scrub. This persistent effect of *p*Hisoderm G-11 is again revealed in Table IV where a comparison is made between the bacterial counts from palmar scrubs during an 11 day soap routine followed by an equal period with *p*Hisoderm G-11. An interval of several days was allowed between the two routines to re-establish the normal bacterial flora of the hands. It will be noted that the counts reached a lower level which were maintained with *p*Hisoderm G-11 in comparison to soap.

Table V indicates that viable bacteria were not trapped beneath a film of G-11 in significant numbers.

The advantages and limitations associated with the use of *p*Hisoderm G-11 as regards

TABLE VIII.—BACTERIAL COUNTS ON GLOVES WORN BY THE VISITING STAFF FOLLOWING A *p*HISODERM G-11 SCRUB*

Number	Length of scrub in minutes	Gloves		Number	Length of scrub in minutes	Gloves	
		Right	Left			Right	Left
1	12	0	0	39	8	0	0
2	12	1	0	40	8	1	0
3	11	1	1	41	8	0	0
4	11	2	1	42	8	0	0
5	10	1	1	43	8	6	2
6	10	2	3	44	8	0	54
7	10	2	0	45	7	3	2
8	10	7	60	46	7	8	37
9	10	6	0	47	7	142	472
10	10	23	0	48	7	0	0
11	10	1	0	49	7	40	20
12	10	283	98	50	7	29	25
13	10	15	29	51	7	5	5
14	10	52	4	52	6	15	—
15	10	1	1	53	6	2	0
16	10	8	1	54	6	34	749
17	10	40	30	55	6	2496	2080
18	10	1	1	56	6	0	0
19	10	10	31	57	6	1	0
20	10	1	4	58	5	1	0
21	10	0	0	59	5	2	3
22	10	0	0	60	5	13	27
23	10	30	61	61	5	0	0
24	10	0	†	62	5	0	0
25	10	19	76	63	5	0	0
26	10	0	3	64	4	2	3
27	9	339	†	65	3	279	80
28	8	10	0	66	3	380	580
29	8	20	10	67	3	146	355
30	8	7	26	68	3	12	5
31	8	30	20	69	3	9	3
32	8	30	†	70	3	10	0
33	8	18	4	71	3	50	54
34	8	0	14	72	3	7	11
35	8	2	1	73	3	0	0
36	8	4	2	74	90″	0	0
37	8	4	7	75	90″	3	8
38	8	6	4				

*Bacteria in 1 c.c. of wash water, multiply by 100 to get the total count from each glove.
†Glove missing.

TABLE IX.—A COMPARISON OF THE AVERAGE BACTERIAL COUNTS OBTAINED FROM THE RESIDENT, SURGICAL NURSING AND VISITING STAFFS FOLLOWING THE SHORT AND LONG SCRUBS*

	Short scrub		Long scrub	
	Right glove	Left glove	Right glove	Left glove
Resident staff and medical students	2.6	3.19	18.1	12.5
Surgical nursing staff	1.8	3.5	10.5	6.8
Visiting staff	50.7	62.7	65.9	75.4

*Bacteria in 1 c.c. of wash water, multiply by 100 to get the total count from each glove.

scrubbing is presented in Tables VI, VII, and VIII. The continuous use of this product by the resident staff, including medical students on delivery service, and the surgical nurses reveals extremely low bacterial counts from their gloves (Tables VI and VII). Table VIII records the bacterial counts from the gloves worn by the visiting staff in line of duty. These counts also remain satisfactorily low. However, scattered exceptions will be noted. The character of the bacterial flora in these cases was not unusual.

Table IX is a summary of the data pertaining to the relative efficiency of the long and short scrubs in the three groups of personnel observed. A short scrub requires 5 minutes or less, whereas a long scrub exceeds 5 minutes.

Table X records the results in the group of 40 medical students who followed the "90 second" scrub routine. Six subjects in this group were unable to continue the *p*Hisoderm G-11 routine, a lapse of an average of 2 days occurring. Although the bacterial counts after the first 90 second scrub following the lapse was higher than the counts for the other students they remained within reasonable limits.

This study does not include cultures for anaerobic organisms nor other fastidious bacteria requiring specialized media. It was assumed that if the hardier organisms succumb to this routine the more delicate ones would not survive.

DISCUSSION

It has been accepted that the surgical scrub with tincture of green soap has been able to affect the bacterial flora of the skin within the limitations of the time allotted and completeness of the exposure of the skin to cleansing. This suggests that the frequency of scrubbing as well as the technique of the scrub itself are the most important factors in attaining surgical cleanliness of the arms and hands, as has been demonstrated by Price. Recently, a third factor has assumed major importance in scrubbing technique, namely, the type of material used for cleansing purposes. This study has been concerned with the efficiency of a relatively new antibacterial agent, *p*Hisoderm reinforced with 3 per cent hexachlorophene (G-11).

As previously indicated, a striking reduction occurred in the number of bacteria obtained from normal control counts on untreated hands as compared to counts obtained after one routine surgical scrub with *p*Hisoderm G-11. Low bacterial counts were also found in a group of surgical nurses who were sub-

TABLE X.—BACTERIAL COUNTS FROM GLOVES WORN BY MEDICAL STUDENTS FOLLOWING THE ROUTINE 90 SECOND SCRUB*

Number	Right glove	Left glove	Number	Right glove	Left glove
1	0	1	21	0	1
2	0	2	22	0	0
3	1	0	23	0	0
4	5	0	24	0	0
5	4	1	†25	79	0
6	2	0	26	0	0
7	0	0	27	0	0
8	9	0	28	0	1
9	2	0	29	1	1
10	0	1	30	1	0
11	2	3	31	1	0
12	0	0	32	0	1
†13	5	3	33	0	0
†14	14	8	34	1	2
†15	5	5	35	1	1
†16	4	24	36	0	0
17	0	0	37	0	1
18	0	1	38	10	1
19	0	0	39	1	6
†20	29	2	40	2	1

*Bacteria in 1 c.c. of wash water, multiply by 100 to get the total count from each glove.
†A 2 day lapse from *p*Hisoderm G-11 routine occurred.

jected to conventional 10 minutes scrubs with *p*Hisoderm G-11 as compared to soap. The elevations in bacterial counts which did occur were higher and more frequent following the soap scrubs. Since these subjects scrubbed frequently each day, the differences noted are felt to be particularly significant.

Repeated quantitative bacterial determinations from gloves and from palmar scrubs show that the effectiveness of *p*Hisoderm G-11 is increased following frequent exposure to the agent. A protective film is formed on the skin which has a persistent antibacterial effect. This is confirmed by failure to detect viable organisms following mechanical removal of the film. This study provides a corollary to the findings of Fahlberg, Swan, and Seastone who were unable to release viable bacteria in significant quantities by experiments devised to remove chemically G-11 from the skin.

The data from three groups of personnel studied reveal that the relative efficiency of the short scrub is dependent upon the frequent use of the detergent. The average bacterial counts of those scrubbing frequently i.e., the medical students, resident and nursing staffs, was lower irrespective of the length of the scrub. In contrast, the visiting staff who were not in daily contact with the detergent exhibited a higher bacterial count even after a long scrub.

This is further emphasized by the bacterial counts obtained from those medical students who performed the 90 second scrub during a period in which they were on delivery service.

These observations indicate that a short surgical scrub could be safely adopted if certain conditions are observed. In brief, these conditions are daily exposure to the detergent and a thorough anatomical scrub. Such a reduction in scrubbing time would be particularly advantageous in obstetrical practice; for on occasion, time does not permit the conventional surgical scrub. In conclusion it would appear that *p*Hisoderm G-11 fulfills the most important requirement of the surgical scrub, namely, that the hands are rendered surgically clean.

SUMMARY

1. Bacteriological data are presented to show the cleansing effectiveness of *p*Hisoderm reinforced with 3 per cent G-11 when used as a preoperative scrub for different groups of medical personnel.

2. A procedure using *p*Hisoderm reinforced with 3 per cent G-11 for surgical scrubbing is described.

3. The persistent antibacterial action of the film of *p*Hisoderm G-11 deposited on the skin has been demonstrated.

4. Frequent exposure to *p*Hisoderm G-11 is essential to maintain a uniform and persistent antibacterial effect.

5. The advantages arising from the use of *p*Hisoderm G-11 for preoperative scrubs as related to obstetrical practice are presented.

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CONGENITAL ESOPHAGEAL ANOMALIES

Review of Twenty-Four Cases and Report of Three

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ATRESIA of the esophagus is a congenital anomaly which is incompatible with life unless surgically corrected. The most common type consists of a blind upper esophageal pouch and a lower esophageal segment which connects the stomach to the trachea (Fig. 1, Vogt's Type III b) (11, 6). This anomaly threatens life in 3 ways: starvation, regurgitation of gastric contents into the trachea, and aspiration of the abundant pharyngeal mucus and saliva. No plan of treatment is satisfactory unless all 3 of these dangers are removed. Gastrostomy and jejunostomy alone are followed by death from respiratory complications. Cervical esophagostomy may provide for disposal of the excess secretions of mouth and pharynx but it is of no avail unless combined with closure of the fistula in the chest. In 1918, Brennemann wrote "The ultimate ideal of all surgical attempts would be . . . union of the upper and lower segments." This was first accomplished successfully in 1941 by Haight and Towsley.

DIAGNOSIS

Atresia should be suspected whenever a newborn infant has excessive pharyngeal mucus. The nursing may be quite characteristic: normal sucking with apparent swallowing, further nursing attempts with regurgitation of unchanged milk, choking, coughing, and cyanosis. The infant may nurse eagerly again and again after the respiratory passages are cleared. The meconium is not noticeably different from normal. The most frequent clinical error in diagnosis in our series was the acceptance of the diagnoses of bronchopneumonia and intracranial birth injuries as explanation of the "feeding problem." Obstruction to passage of a catheter readily demonstrates the obstruction. X-ray examination after a small feeding of lipiodol or after instillation of air with the infant inverted may confirm the diagnosis.

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REVIEW OF CASES

The clinical diagnosis was confirmed by x-ray studies in 14 of the 21 cases of atresia (Figs. 2, 3, and 4). Autopsy diagnosis of this lesion (IIIb) was made 10 times, 3 times confirming the clinical diagnosis and 7 times disclosing a previously unrecognized anomaly (Fig. 5).

There were associated other congenital anomalies in 8 of the 21 cases of atresia as follows: club feet and absence of the kidneys; bilateral hydronephrosis and hydroureter; deformity of the thumb; spina bifida occulta; imperforate anus; imperforate anus and rectovesical fistula; hypospadias; internal hydrocephalus. In only 5 of these was the other anomaly of vital importance. These findings correspond to those of Humphreys and others (3, 7, 10). A defeatist attitude is not warranted in such cases because the chance of there being other important anomalies is only about 1 in 4.

The association with imperforate anus deserves special consideration as there are 2 such

TABLE I.—TWENTY-FOUR CASES OF ESOPHAGEAL ANOMALY AT BUFFALO CHILDREN'S HOSPITAL DURING THE 10 YEARS, 1940 TO 1949

	No. cases	Results
Stenosis	3	2 still living
Atresia alone Vogt II	1	Clinical and x-ray diagnosis. No autopsy
Atresia with upper fistula Vogt IIIa	2	One lived only 4 hrs. Autopsy diagnosis. The other died on 3rd day of life, after operation
Atresia with lower fistula Vogt IIIb	18	16 died. One survived for 21 months —"Case 1." One survived and is apparently normal—"Case 2"

There have been 2 cases of congenital tracheoesophageal fistula without atresia in the Buffalo Children's Hospital, not included in this series, one in 1931, the other in 1950.

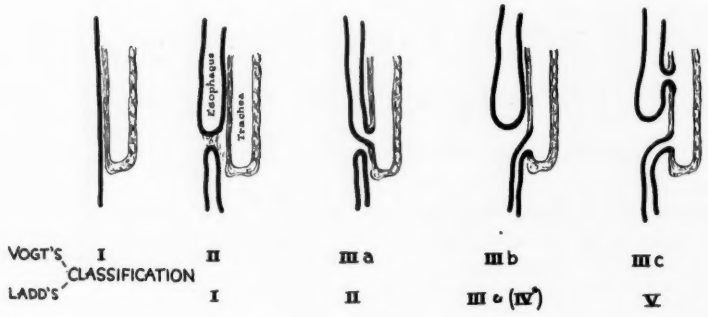

Fig. 1.

cases in this series. *Marked abdominal distention during the first 2 days after birth is apparently not due to imperforate anus alone but is apt to occur when there is an associated tracheoesophageal fistula.*

PATHOGENESIS

The embryologic basis for this defect is apparently one of faulty timing of growth and developmental processes. The primitive respiratory tract forms as a ventral groove in the esophagus; it is normally separated from the esophagus by invagination of lateral septa and then there is rapid longitudinal growth of the trachea. If this rapid longitudinal growth occurs before separation is complete, one of these anomalies may result.

ETIOLOGY

Factors of etiology are not well understood. Mackenzie described a typical case; the father stated that a former wife had given birth to a child who died after 19 days with exactly the same symptoms. Meckel observed that the same male occasionally produces a similar deformity in the offspring by different women. Mackenzie also calls attention to Hirschsprung's observation of 4 cases of esophageal atresia in less than 7 months in a town of only 180,000 inhabitants and Ilott's finding 2 cases within 3 weeks in a country district near London. Nine infants of our 24 cases were born during the period of 13 months between November 1942 and December 1943, 8 Type IIIb and 1 Type II. Three were born in December 1941, all atypical cases, 2 stenoses and 1 Type IIIa. This peculiar time grouping of cases suggests that the condition may be caused by prenatal influences rather than heredity. Two infants had the same unusual family name, and 2 were twins (only 1 of each pair of twins in this series). Further study is being made of these possible etiologic factors.

Eight of these infants with atresia were operated upon by 4 surgeons. One had gastrostomy alone in 1943 (Fig. 2) and died at operation. Three had transpleural operations and died postoperatively. Four had extrapleural anastomoses; of these there were 2 postoperative deaths, 1 lived for 21 months, and 1 survived. Three were operated upon by one of us (R.K.B.) and are here reported.

CASE 1. R. G., 121577, male infant (2), was born on July 22, 1947. Birth weight was 7 pounds 2 ounces. The mother gave a history of brucellosis for 4 years prior to this pregnancy; there were miscarriages in 1942 and 1945.

The baby appeared normal but vomited everything offered by mouth. Choking and cyanosis were associated with feedings. Between feedings, because of an excess of mucus, suction was necessary. An unsuccessful attempt was made to pass a gavage tube. Roentgenograms taken after instillation of lipiodol showed the esophagus ending in a blind pouch at the level of the second thoracic vertebra, and also demonstrated the presence of gas in the stomach and intestines (Fig. 6). A diagnosis of Vogt IIIb anomaly was made.

At 15 days of age, the lesion was exposed by a right extrapleural operation with resection of several ribs under local procaine anesthesia. The balloon-like upper segment of esophagus was found without difficulty, somewhat beyond the midline (Fig. 7). The lower segment was clamped and cut close to the trachea and the tract into the trachea was closed with a transfixion ligature. The two ends of the esophagus were then opened, threaded on a No. 10 catheter and an anastomosis was made with in

Fig. 2.

Fig. 2.* C.C., 90330. Infant died 4 days after birth, with asphyxia due to aspiration during attempted gastrostomy (1943). Note blind esophageal pouch filled with lipiodol.

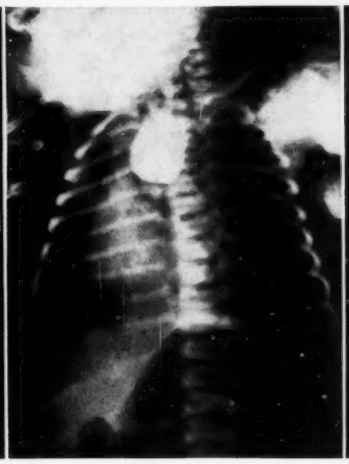

Fig. 3.

Fig. 3. J.S., X32-900. Infant died 2 days after birth (1943).

Fig. 4.

Fig. 4. G.W.F., 105015. Infant died 13 days after birth. Surgery advised on the fifth day but not undertaken (1946).

terrupted cotton stitches. The lower segment was small, thin, and friable, especially on its anterior surface where it had been obliquely fused with the trachea. In this area, the stitches caused a longitudinal tear which was closed with interrupted stitches. Positive pressure oxygen inhalations were used, with frequent aspiration of the throat and trachea. The lung was expanded as the chest wound was sutured and it was noted to be less atelectatic than at the beginning of the operation. A catheter was left in the esophagus to the stomach, but this was promptly vomited up. Gastrostomy was performed 24 hours later, a simple Witzel operation under local procaine anesthesia. An esophageal fistula developed at the site of the chest operation.

When the infant was 2 months old, lipiodol instillation showed the esophagus angulated to the right and posterior. Most of the lipiodol passed into the stomach with only slight delay at the cardia. A small amount of oil pooled at the level of the fourth dorsal vertebra and then passed posteriorly out the fistulous tract. No oil passed into the trachea. The chest wound healed and choking spells became frequent and severe. Aspiration pneumonia responded to sulfonamides given by gastrostomy tube.

At the age of 3 months, he was readmitted for a second chest operation. The esophagus was identified and a ureteral catheter and silk string were threaded through the nose, esophagus, and stomach and brought out the gastrostomy opening by means of an iron bead and a magnet (9). The string served as a guide for retrograde bouginage. An opening that admitted a No. 12 French Tucker bougie was maintained but the baby continued to refuse food by mouth. He developed well on gastrostomy feedings and began to walk at 11 months. There seemed to be a valve-like effect at the site of scar; swallowing was obstructed but upon occasions he vomited gastric contents freely. The esophageal fistula to the skin of the right scapular region remained patent until the age of 18 months when it closed. The child chewed through and removed the silk thread being used for weekly bouginage. The excess of pharyngeal mucus recurred and respiration became stertorous.

At 19 months, another operation was performed which consisted of freeing the esophagus from its attachment to the deformed ribs, threading it again with silk thread, and of removing the upper lobe of the right lung which was found to be filled with small abscesses. The fistula in the scapular region reappeared and the general status was unchanged.

At 21 months of age, the thorax was again opened and the esophagus was dissected free of the deformed ribs with great difficulty. It was also firmly adherent to the trachea and right main bronchus. During the dissection a small opening was made in the trachea and immediately snugly closed with interrupted sutures of No. 60 cotton. The scarred portion of esophagus was excised and an end-to-end anastomosis was made. The anesthetist aspirated tracheal mucus repeatedly during the operation and several times postoperatively. Death occurred on the second day from massive atelectasis, confirmed at autopsy.

Case 2. A. C., 142159, girl infant, premature, jaundiced (patient of Dr. Richard A. Downey), born April 23, 1949, was transferred to the Buffalo Children's Hospital at the age of 7 days when she weighed 4 pounds 4 ounces. The diagnosis had been

*Figures 2, 3, and 4 by courtesy of Dr. Newton D. Scatchard, roentgenologist, Buffalo Children's Hospital.

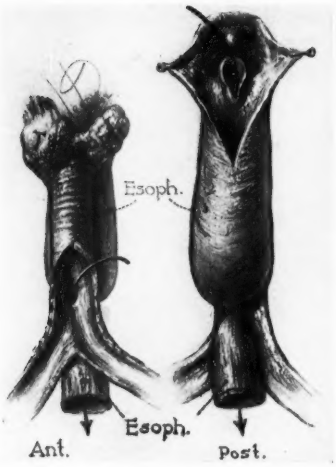

Fig. 5. L 83894 A831. Drawing of autopsy findings. The infant died on the seventh day. There was much pharyngeal mucus and cyanosis. The clinical diagnosis was atelectasis and pneumonia. The correct diagnosis, esophageal atresia with tracheoesophageal fistula (Vogt type IIIb) was not suspected during the life of the infant (1942). Courtesy of Dr. Kornel Terplan, Professor of Pathology, University of Buffalo School of Medicine.

suspected because of much mucus in the throat and prompt regurgitation of formula with choking and cyanosis. It was confirmed by obstruction to the passage of a catheter and by x-ray examination (Fig. 8). The fluid status was apparently satisfactory.

Operation was performed at once, right extrapleural thoracotomy through the bed of the third rib. The azygos vein was cut between ligatures and the two segments of esophagus were exposed without

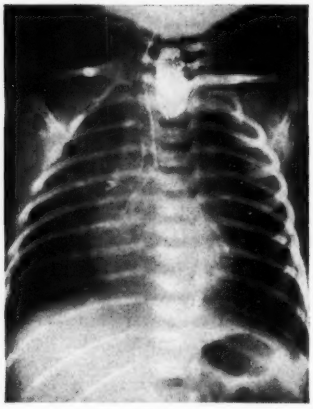

Fig. 6. Roentgenogram of Case 1. Courtesy of Dr. Roy E. Seibel, Roentgenologist, Deaconess Hospital.

difficulty (Fig. 7). The communication of the lower segment to the membranous portion of the trachea was clamped longitudinally, cut, and closed with 2 figure of 8 cotton stitches. The blind pouch above was then opened and an unsuccessful attempt was made to anastomose the mucosa of the two segments of esophagus. The ends were then trimmed and a full thickness anastomosis was performed over a catheter with interrupted No. 60 cotton stitches. A small longitudinal rent in the end of the lower segment was closed and a complete ring of reinforcing mattress sutures was made in the muscularis. *The catheter was removed and the anastomosis was proved to have no leaks by filling the wound with saline and pumping oxygen through a pharyngeal catheter into esophagus and stomach.* The thorax was closed without drainage.

Three days later a Witzel gastrostomy was performed. This was used for feeding from the following day until the tenth day after the esophageal anastomosis. Feedings were then taken by mouth. The gastrostomy wound healed promptly without leakage after removal of the tube.

Growth and development are normal to the age of 13 months. There is no difficulty in swallowing. Fluoroscopy and x-ray examination of the esophagus show no obstruction or deformity.

CASE 3. C. M. S., 144523, girl infant (patient of Dr. William J. Orr), born 1 month prematurely on July 5, 1949; the birth weight was 5 pounds 2 ounces. On the second day of life there was persistent vomiting. The correct diagnosis, atresia of esophagus Type IIIb, was at once suspected and confirmed by x-ray examination. The general condition was good but there was x-ray evidence of pneumonia of the right upper lobe.

Operation was performed on the third day of life, exposing the esophageal segments through a right extrapleural thoracotomy with resection of the fourth rib. Procaine 0.5 per cent locally and nitrous oxide were both used in small amounts. Oxygen with positive pressure was supplied. The parietal pleura was stripped posteriorly to the vertebral column and the azygos vein was severed and ligated. The upper pouch and the lower esophageal segment were isolated and the fistula into the trachea was cut over a hemostat. The stump of the fistula was then closed by transfixion ligation with No. 20 and No. 60 cotton. A stab wound was then made in the upper blind pouch and the two segments were anastomosed over a catheter with a large number of No. 100 white cotton sutures. *The line of suture was found to be competent by testing under saline solution while the anesthetist passed oxygen down the reconstructed esophagus into the stomach.* The chest wound was closed in layers while the anesthetist re-expanded the lung. A Witzel gastrostomy was performed on the following day.

On the second day after the chest operation, the respirations became labored and a diagnosis of fluid in the right chest was confirmed by x-ray examination.

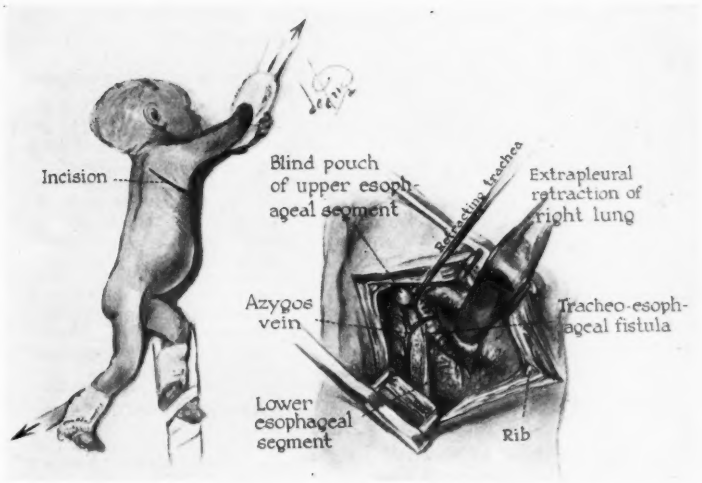

Fig. 7. Operative exposure. In Case 1 several ribs were resected. Resection of 1 rib only (3rd or 4th), as illustrated, gave adequate exposure in Cases 2 and 3.

Thoracentesis yielded only about 5 cubic centimeters of serosanguineous fluid. The infant died a few hours later. At the autopsy the right chest was full of brownish fluid. There was a leak at the line of anastomosis where sutures had torn through. There were also an internal hydrocephalus and meningitis which were previously unsuspected.

This death was due to an error in technique; the anastomosis was not competent. However the hydrocephalus was incompatible with normal life.

DISCUSSION

The diagnosis of esophageal atresia is easily made if the possibility is considered. Report that a newborn has much mucus in the mouth and throat should arouse suspicion. There is, of course, prompt regurgitation of unchanged formula, but this may be overlooked by the attendants as the normal spewing of infancy. Choking and cyanosis are common. Bronchopneumonia is the usual complication. Obstruction to passage of a gavage tube proves the diagnosis. X-ray examination with lipiodol shows the blind pouch. In such cases, gas in the gastrointestinal tract indicates the presence of a tracheal fistula to the lower segment.

These cases are hopeless without surgery. Surgery is withstood well. Pneumonia is not a contraindication; the anesthetist does much during the operative session to clear the respiratory tract and the procedure relieves the infant of the abundance of pharyngeal mucus.

SUMMARY

1. Esophageal atresia should be suspected when a newborn has much mucus in the throat, feeding difficulties and bronchopneumonia. It is proved by obstruction to passage of a catheter and by x-ray examination.

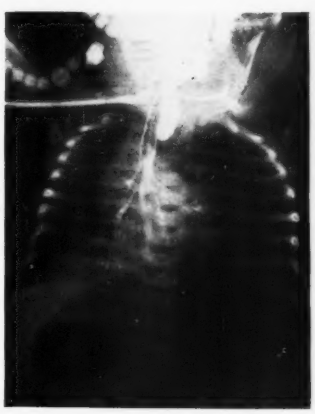

Fig. 8. Roentgenogram in Case 2. Note that lipiodol outlines the fistula. Courtesy of Dr. John M. Barnes, roentgenologist, Millard Fillmore Hospital.

2. Ten years' experience (1940 to 1949) with esophageal anomalies at the Buffalo Children's Hospital is summarized, represented by a total of 24 cases.

3. In cases of imperforate anus with abdominal distention during the first 2 days of life a coexistent tracheoesophageal fistula should be suspected.

4. Surgical correction offers the only hope of survival, and should be undertaken within the first few days of life.

5. The management of choice for the most frequent anomaly (IIIb) is first an extrapleural operation through the bed of either the third or fourth rib on the right side, with closure of the tracheal fistula and end-to-end anastomosis of the esophagus followed by gastrostomy a day or two later.

6. Insufflation of the esophagus with oxygen while the anastomosis is inspected under physiologic saline solution is offered as a useful but not infallible test of the competence of the suture line.

7. The occurrence of several cases within a period of a few months suggests that the anomaly may be environmental rather than truly hereditary. Search for possible etiologic factors during the early weeks of gestation seems warranted.

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THE VALUE OF SURGICAL TREATMENT OF CORONARY ARTERY OCCLUSION BY IMPLANTATION OF THE INTERNAL MAMMARY ARTERY INTO THE VENTRICULAR MYOCARDIUM

An Experimental Study

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MANY attempts have been made to augment the circulation of the ventricular myocardium in cases of coronary artery sclerosis. Much of the previous work has been done experimentally and a considerable part of it has been carried out on human subjects.

In the past, there have been four main approaches to this problem, namely: (a) The application of a graft to the surface of the heart, such as pectoral muscle (1), omentum (17), and lung (4, 14). (b) Cardiopericardiopexy: The principle of this procedure was to obtain fresh blood supply from the parietal pericardium by the creation of granulomas between the visceral and parietal pericardia. This was first attempted by Beck (3, 20), using a burr, beef bone, and asbestos powder. Others such as Thompson, Heinbecker and Barton, and Rakov, have inserted various irritating substances into the pericardium. (c) Cardiac vein ligation: This was first suggested by Gross (10, 11) and carried out by Fauteux (5, 6, 7, 9). By vein ligation it was thought that interarterial anastomoses would be opened and that the ventricular muscle would receive increased oxygenation by means of the thebesian canals. (d) Arterialization of the coronary venous system: In this procedure, arterial blood is brought to the coronary sinus by means of an anastomosis. The operation has been performed by various authors, namely, Beck (2), Stenstrom, Fauteux (8), Roberts and associates, and has been applied clinically by Beck.

A different approach to vascularization of the ventricular myocardium was reported by one of us (A.M.V.) in 1946 and 1947 (23, 25). The left internal mammary artery was employed as a source of fresh arterial blood for the ventricular myocardium. The internal mammary artery was detached from its position on the chest wall and placed within a tunnel in the ventricular myocardium. It was shown that the implanted internal mammary artery anastomosed with the left coronary circulation at the end of 3 months. Proof of anastomosis was made by means of radiopaque injection mass, roentgenogram, serial section, and plastic cast (Figs. 1 to 6). The various factors in the technique of implantation of the internal mammary artery into the ventricular myocardium were studied in considerable detail. It was found that the shorter the length of artery freed from its chest wall attachment, the greater were the chances of the implanted artery remaining patent and forming an anastomosis with the coronary circulation (24).

In the past year, further studies have been conducted in order to ascertain: (1) the degree of protection afforded by the implantation against infarction and mortality; (2) the factors which might influence the formation of a functioning anastomosis.

PROCEDURE

Various procedures were carried out in an effort to discover some of the factors which were responsible for anastomosis, and also

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Fig. 1. Cannula in the left internal mammary artery 13 months after the artery had been implanted in the wall of the left ventricle. Note that the injection fluid has also flowed into the chest wall.

some of the factors which caused certain arteries to thrombose. It was thought that if the implanted internal mammary artery were placed in ischemic ventricular muscle, this might stimulate the artery to send out new branches. Accordingly, certain experiments were done in which a branch of the left coronary artery was constricted prior to the implantation of the internal mammary artery.

Another group of experiments was conducted in an attempt to create venous congestion in the area of implantation by ligation of the great cardiac vein. This was done to determine whether it would influence the number of anastomoses.

In another group, a study was made of the value of heparin in preventing thrombosis of the implanted internal mammary artery.

A careful analysis was made as to the depth of implantation, the bleeding activity of the implanted intercostal branches and the apical adhesions of the heart. In order to determine the efficacy of an anastomosis, the anterior descending branch of the left coronary artery was ligated at its origin in every animal from 6 to 24 weeks after internal mammary artery implantation. An additional control group of 10 animals was studied after ligation of the anterior descending branch of the left coronary artery without an internal mammary artery implant. Hearts were studied by injection of the internal mammary artery with Schlesinger's solution, by multiple microscopic sections about the site of implant and by roentgenographic observations.

EXPERIMENTS

Standard internal mammary artery implantation (group A1). In all experiments, dogs were used under intravenous nembutal anesthesia, and an intratracheal tube with a positive pressure was employed. The left thorax was opened through the fifth intercostal space, and the internal mammary artery freed from the chest wall from the fourth to sixth costal cartilages, inclusive. At the level of the sixth costal cartilage the internal mammary artery was doubly ligated and severed. The fourth and fifth intercostal branches were tied with catgut and severed. Six cubic centimeters of 1 to 1,200 solution of nupercaine were injected into the pericardium. After a few minutes the pericardium was opened, a cotton suture was placed in the apex and the myocardium incised in two places, approximately 2 centimeters apart. By means of a curved hemostat the internal mammary artery was pulled through the superior incision out of the inferior incision where it was fixed by the original stay suture. Prior to pulling through the artery, the sixth intercostal artery was divided, without ligature, and drawn into the tunnel of the myocardium. The lungs were re-expanded and the wound closed in layers about a catheter, the residual air in the thoracic cavity being removed by means of catheter aspiration.

Partial occlusion of the anterior descending branch of the left coronary artery (group A2). In 11 animals, after implanting the internal mammary artery into the left ventricular

myocardium, a small branch of the anterior descending branch immediately proximal to the site of the implant was partially occluded. Partial occlusion was accomplished by means of a silk ligature tied around the artery, with accompanying vein, and a No. 23 gauge needle. After the ligature had been tied the needle was removed.

Cardiac vein ligation (*group A3*). In 9 animals the great cardiac vein was ligated close to the coronary sinus. At the same operation the internal mammary artery was implanted. Four of these animals (*group A4*) were treated with heparin in Pitkin's menstruum for 5 days. This maintained the clotting time at twice the normal levels for 5 days.

EXPERIMENTAL RESULTS

Operative mortality. Of the 42 animals subjected to the implantation operation, 16 died prior to being subjected to anterior descending branch ligation. Fourteen deaths occurred in group A1, one in group A2, one in group A3, and none in group A4. Of the 16 animals, 10 died as a result of pleural effusion or empyema. In 6, the cause of death was not definitely established, but distemper was suspected in some.

In the dog, it is very difficult to control pleural effusion following transthoracic procedures. This is due, partly, to the dog's intolerance of continuous intrathoracic suction, and partly to an incomplete mediastinum. Most of the animals that died as a result of fluid accumulation showed fluid to be present in both pleural cavities. This complication was satisfactorily controlled by catheter aspiration and re-expansion of the lungs on the operation table at the time of wound closure.

Proof of anastomosis. In previous experiments, reported in 1946, 1947, 1949, (23, 24, 25), an anastomosis was considered to be present only when visible filling of the coronary circulation was achieved by the injection of Schlesinger's solution. In this series, more detailed studies have been carried out, and microscopic sections showed the injection mass in many myocardial vessels. In several instances the injection mass was in the deep vessels and was not present on the surface of the heart. The injections through the internal mammary artery which visibly filled the surface coronary arteries of the left ventricle have been termed "macroscopic anastomoses." Those injections in which there was only microscopic evidence of filling have been termed "microscopic anastomoses." It should be noted that Schlesinger's solution has been used because it will not pass through vessels which are smaller than 40 microns in diameter (arterioles).

Fig. 2. Demonstrates that only the left coronary vessels were injected to the complete exclusion of the vessels of the right ventricle.

Results from animals subjected to internal mammary artery implantation. In a previous publication (24) it has been shown that the greatest number of anastomoses occurred when the internal mammary artery was freed from the fourth to sixth intercostal cartilages, inclusive. It should be noted that all animals reported in the present groups have undergone this standard operation, with various additional procedures.

Group A1.—Standard implantation. In this group there were 6 animals which underwent the standard internal mammary artery implant procedure. Two of the 6 survived anterior descending branch ligation; one showed a "macroscopic anastomosis" and no

Fig. 3. Roentgenogram of the left coronary tree which has been filled by injecting the left internal mammary artery 99 days after it was implanted into the left ventricular wall.

infarct. In the latter animal, the anterior descending branch of the left coronary artery was ligated 1 centimeter from its origin; this ligature failed to include the septal branches. Three of the 6 implanted internal mammary arteries were found to be patent within the myocardium; in 2 of these an anastomosis was not demonstrated by injection of Schlesinger's solution.

Group A2.—Standard internal mammary artery implantation, plus partial occlusion of the anterior descending branch, vein and artery, plus pericardial fat wrap. Eleven animals were subjected to anterior descending branch ligation, 8 of which survived, 5 without infarction; 3 were proved to have "macroscopic" and 2 "microscopic anastomoses." Two of the 3 animals which survived infarction showed no evidence of an anastomosis, and the other showed evidence of "microscopic anastomosis." Thus, the total number of demonstrable anastomoses in this group was 6 out of 11 (54.5 per cent). There were 8 of the 11 in which the internal mammary artery was patent within the myocardium (72.7 per cent).

Group A3.—Standard internal mammary artery implantation, plus ligation of the great cardiac vein. Five animals were subjected to anterior descending branch ligation. There were no survivors with or without infarction. There were 3 animals in which the internal mammary artery had been thrombosed and recanalized; these proved to have a "microscopic anastomosis." In one of the 2 animals not showing a demonstrable anastomosis, the internal mammary artery was shown to be patent within the myocardium; in the remaining animal the vessel was occluded.

Group A4.—Standard internal mammary artery implantation, plus great cardiac vein ligation, plus heparin. Four animals were subjected to anterior descending branch ligation, 3 of which survived without infarction. Two of these showed a "macroscopic" and 1 a "microscopic anastomosis." The animal which failed to survive showed a patent artery within the myocardium.

Control group.—In order to estimate the degree of protection afforded by an internal mammary artery implant, a group of control animals was studied. Ten dogs had the anterior descending branch of the left coronary artery ligated at its origin. The site of ligation in the control group was in exactly the same location as that carried out in groups A1, A2, A3, and A4. All the ligatures placed on the anterior descending branch were checked as to location at postmortem examination and each left coronary artery was probed to make certain that the ligature completely occluded the vessel at its origin. In the control group, no implant of the internal mammary artery was carried out.

Of the 10 animals subjected to anterior descending branch ligation, 8 died within 48 hours; 1 lived 11 days and died showing a 5 by 5 centimeter infarct on the anterior wall of the left ventricle. The tenth dog was sacrificed after 21 days, showing a 5 by 4 centimeter infarct of the anterior wall of the left ventricle.

Summary of experimental results (Table I). The survival rate after anterior descending branch ligation was: 33.3 per cent in group A1, 72.7 per cent in group A2, 0 per cent in group A3, 75 per cent in group A4, 50 per

Fig. 4. Serial section showing internal mammary artery lying in the myocardium 13 months after implantation. The large indentation in the arterial wall represents a beginning branch.

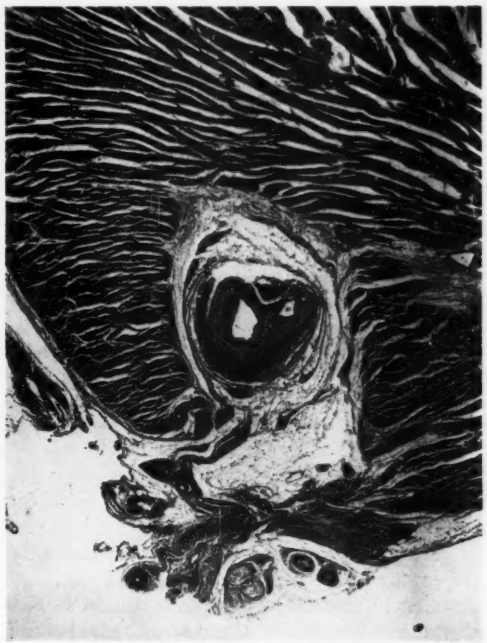


Fig. 5. Serial section of same artery as is illustrated in Figure 4. The branch has developed into a second artery. The new artery is seen lying alongside of the parent vessel.

cent in the total group as compared with 10 per cent survival rate of the control group.

The survival rate without infarction after anterior descending branch ligation was: 16.6 per cent in group A1, 45.5 per cent in group A2, 0 per cent in group A3, 75 per cent in group A4, 34.2 per cent in the entire group as compared with the control, in which there were no survivors without infarction.

The total number of proved anastomoses was 16.6 per cent in group A1, 54.5 per cent in group A2, 60 per cent in group A3, 75 per cent in group A4, 50 per cent in entire group.

Of the 26 animals studied (Table I), there were 19 animals in which the internal mammary artery was open within the myocardium after 3 months or longer. Thirteen of the 19 animals with a patent implanted artery were shown by Schlesinger's solution injection to have an anastomosis between the implanted internal mammary artery and the left coronary circulation. There were 6 animals in which the internal mammary artery was shown to be open within the heart, but in which injection of Schlesinger's solution failed to show any evidence of anastomosis. It is believed that an artery lying within the myocardium which remains patent for 3 months or longer must have some degree of circulation. As previously mentioned, the caliber of the vessels permitting circulation in such an artery may be too small to be demonstrable by Schlesinger's solution. Furthermore, it is assumed that any vessel that is completely occluded, with no anastomotic circulation, will develop within its lumen, back to its nearest functioning branch, a solid thrombus which would fail to recanalize. That the caliber of the anastomotic channels of the 6 animals must have been smaller is further suggested by the fact that none of

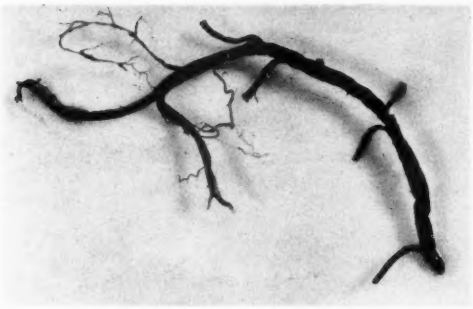


Fig. 6. A cast has been made by injecting the internal mammary artery with a plastic substance 10½ months after implantation into the left ventricular wall. The small sharply cut off branches to the right are intercostals tied with cotton. The fine aborizations to the left have developed within the heart muscle.

these animals survived anterior descending branch ligation. This will be discussed at greater length when considering the degree of protection afforded by internal mammary implantation. It might be considered that arteries lying within the heart would fail to thrombose because of the massaging action of this organ. This concept, however, cannot be offered as an explanation of the vessels which were found to be open so frequently within the myocardium, since other vessels receiving the same massaging action became solidly thrombosed. It therefore seems reasonable to assume that an internal mammary artery implanted into the left ventricle which presents a patent lumen at the end of 3 months or longer must have some degree of anastomosis. If one adds the 6 animals with patent internal mammary arteries to the group of 13 with demonstrable anastomoses, 19 of the 26 animals examined could then be considered to have developed anastomosis (73 per cent). It is possible that under a proper stimulus, such as a slowly developing coronary occlusion, these anastomotic channels could enlarge sufficiently to form anastomoses demonstrable by the method employed (Schlesinger's).

Comment. Due to the relatively small number of animals in each group, it is not possible to draw any definite conclusions as to the value of the different procedures in stimulating anastomosis. Certain impressions, however, have been gained. It would seem, from analysis of group A2, that the percentage of anastomoses was increased following the pre-

TABLE I.—SUMMARY OF FREQUENCY OF ANASTOMOSES WITH VARIOUS IMPLANTATION OPERATIONS. THE VALUE OF ANASTOMOSIS IN PROTECTION AGAINST CORONARY ARTERY OCCLUSION

Group	No. of animals	Survivors of anterior descending branch ligation				No. of proved anastomoses (Schlesinger's)				Total anastomoses (Including specimens with patent implantation of I.M. artery)	
		Total		Without infarct	With infarct	Total		Macroscopic	Microscopic		
		No.	Per cent			No.	Per cent			No.	Per cent
A1 Standard I.M. artery implantation	6	2	33.3	1 (macroscopic)	1 (poor tie)	1	16.6	1	0	3	50
A2 Standard implant plus partial occlusion of A.D.B.	11	8	72.7	5 (2 microscopic 3 macroscopic)	3 (1 microscopic)	6	54.5	3	3	8	72.7
A3 Standard implant plus cardiac vein ligation	5	0	0	—	—	3	60	0	3	4	80
A4 Standard implant plus ligation of great cardiac vein plus heparin	4	3	75	3 (1 microscopic) (2 macroscopic)	0	3	75	2	1	4	100
Total	26	13	50	9	4	13	50	6	7	19	73
Control	10	1	10	(with infarct)							

I.M.—Internal mammary artery
A.D.B.—Anterior descending branch, left coronary artery

liminary constriction of a portion of the anterior descending branch of the left coronary artery at the time of implantation. This impression has been further substantiated by the survival without infarction of 1 of these animals after ligation of both the anterior descending and the circumflex branches of the left coronary artery. These results are not surprising since it has been shown by other investigators (3, 16) that myocardial ischemia is a stimulus to the development of anastomosis. In group A_3, there was no evidence that cardiac vein ligation increased the number of functioning anastomoses. In group A_4, in which heparin was added, there appeared to be a definite increase in the number of anastomoses. It is interesting to note that in group A_3 the anastomoses that developed were of the microscopic type, and actually, were developed through recanalization of a thrombus in the internal mammary artery. In group A_4, in no instance was the internal mammary artery thrombosed in any part. Since the heparin was administered during the first 5 postoperative days, it must be assumed that the thrombus developed during this early postoperative period.

Findings in animals developing anastomoses. In this group, as in the previously published group, serial sections through the site of implant were made in cases of demonstrable "macroscopic anastomosis" (Fig. 7). A study of these serial sections revealed branching of the implanted internal mammary artery. These branches were filled with injected Schlesinger's solution (Fig. 8). Differentiation of the injection mass from red blood cells was not difficult. Arteries of relatively large size in the myocardium, near the implanted internal mammary artery, were seen to be filled with the injection mass (Fig. 9). When the anastomosis was of "macroscopic" size, the injection mass was visible in the small vessels throughout the left ventricular myocardium, extending from the epicardial surface to the endocardial surface (Fig. 10). Sections from the interventricular septum and right ventricle showed the injection mass in numerous arterioles of these structures.

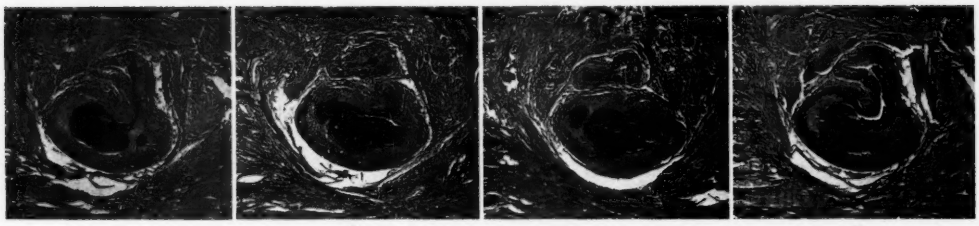
In those cases developing only "microscopically" demonstrable anastomosis (Fig. 11), the injection mass was not so widely distributed, it being present in some myocardial vessels and absent in others. It should be noted that in all animals showing "microscopic anastomosis" the internal mammary artery had become thrombosed and recanalized.

Fig. 7. Injection of internal mammary artery with Schlesinger's solution 89 days after implantation. Note filling of left coronary circulation with dye.

A study of Table II reveals that the highest percentage of anastomoses occurred when the internal mammary artery was placed in the inner two-thirds of the myocardium. Of the 13 animals developing demonstrable anastomoses, 2 of the animals with implants in the outer third, 6 with implants in the middle third, and 1 with an implant in the inner third survived anterior descending branch ligation. Thus, implants at all depths of the myocardium protect against this ligation. The location of the anastomosis in the myocardium seems to be related to the frequency of

TABLE II.—DEPTH OF IMPLANT AS A FACTOR IN ANASTOMOSIS

Depth of implant	No. of animals	Animals with anastomosis	
		No.	Per cent
Outer third	7	2	28.6
Middle third	14	9	64.3
Inner third	2	2	100



a b c d

Fig. 8. Serial sections of internal mammary artery 89 days after implantation into myocardium. Schlesinger's injection mass is shown as a dark shadow. Note, a, area of indentation showing new branching; b, new branch alongside parent artery with a second artery commencing to form to left of lumen; c, newly formed arteries lying alongside parent artery; d, elastic stain showing internal elastic lamina in new branch.

anastomoses, but does not play a part in the degree of collateral circulation developed.

DISCUSSION

In previous publications it was shown that an anastomosis occurred between an implanted left internal mammary artery and the left coronary circulation. Many technical factors concerning the frequency of anastomosis were studied. The proof of anastomosis was concluded by the visible and microscopic presence of Schlesinger's solution filling the coronary vessels after its injection into the internal mammary artery. Further proof of an anastomosis was elicited by means of serial sections, roentgenograms and plastic casts. Very little was known concerning the value of such anastomosis in protecting against coronary artery occlusion. We now believe that possibly three types of anastomoses occur between the implanted mammary artery and the left coronary circulation. These differ according to the size of the vessels which form the anastomosis. The first type (macroscopic) is formed by large vessels which permits of an immediate visible filling of the vessels of the left ventricle by the injection mass. The second type (microscopic) is only discernible by the presence of the injection mass throughout the myocardium which is seen in the microscopic section. The third form of anastomosis is one which is assumed to be present when an implanted internal mammary artery lies within the ventricular myocardium for 3 months or longer without having its lumen occluded by thrombus.

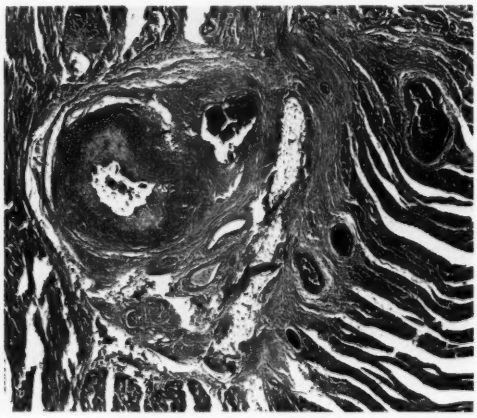
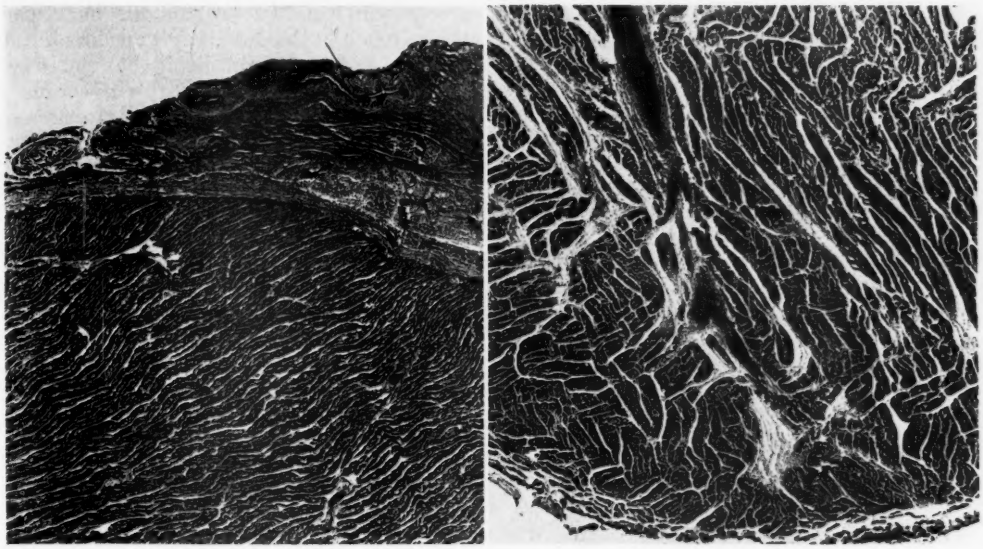


Fig. 9. Section through site of internal mammary implant 127 days after implantation. Note: (a) patent internal mammary artery; (b) daughter branch lying alongside containing dark injection mass; (c) fine vessels in surrounding myocardium filled with dark injection mass.

The value of anastomosis. This study has been made in order to determine whether the arterial blood supply brought to the myocardium by the internal mammary artery will protect a heart against failure after coronary artery occlusion. If an internal mammary artery implantation is to be of value in the treatment of angina pectoris in humans, it is important to determine whether it will supply sufficient blood to the left ventricle to compensate for left coronary artery occlusion. An estimation of the value of protection in the experimental animal has been gauged by the mortality rate and by the presence or absence, both grossly and microscopically, of ventricular infarcts. On analysis, it will be seen from Table I that in every instance of macroscopic anastomosis, infarction did not



a b

Fig. 10. Section of myocardium after injection of internal mammary artery with Schlesinger's solution 60 days after implantation. a, Shows vessels of epicardium filled with the injection mass. b, Shows the vessels in the region of the endocardium which are filled with injection mass.

occur following ligation of the anterior descending branch of the left coronary artery (Fig. 12). It would also appear possible for a recanalized vessel to deliver sufficient blood to the ventricular muscle in certain cases to prevent death and ventricular infarction (Fig. 11). The degree of protection seems to depend on the caliber of the anastomotic channels, which must govern the amount of blood delivered to the ischemic myocardium. In the control group of animals, death occurred in 90 per cent, and infarction in the surviving 10 per cent, following anterior descending branch ligation.

In comparing the various procedures which were carried out, it would seem that the simple standard internal mammary artery implantation, as previously reported, is the procedure of choice, possibly supplemented by the use of anticoagulants. Since it has been shown that the injection mass finds its way into the interventricular septum from the left ventricle and, in certain cases, into the right ventricle, it is logical to assume that, given time, the internal mammary artery can revascularize the entire ventricular musculature.

In coronary artery disease as it occurs in the human, the portion of coronary artery most frequently affected is that closest to the aorta. The more distal vessels, and particularly the deeper arterioles, most frequently

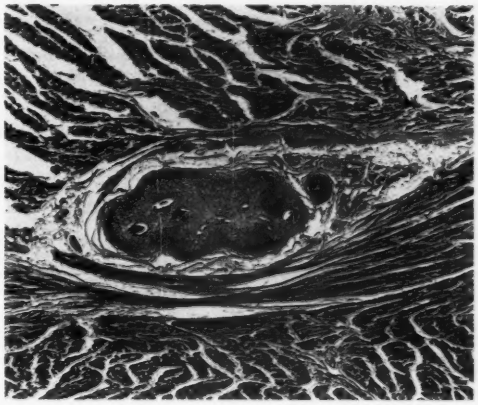


Fig. 11. Note implanted internal mammary artery 141 days after implantation. The implanted internal mammary artery contains recanalizing thrombus. The injection mass entered the recanalized channels and filled adjacent myocardial vessel. Animal survived anterior descending branch ligation without infarct.

Fig. 12. Implantation of internal mammary artery in wall of left ventricle 60 days before injection. Wall of left ventricle sectioned after animal had survived ligation of both anterior descending and circumflex branches of left coronary. Note absence of infarct.

escape disease. Anatomically, it is well established that there are terminal branches of the right and left coronary arteries which find their way to the apex of the heart. Thus, the apex becomes an ideal location for this implantation. An anastomosis occurring between the implanted internal mammary artery and the apical vessels should, theoretically, reach the vessels of the major coronary circulation. We have witnessed this during the injection of an implanted internal mammary artery with Schlesinger's solution: the injection mass has been observed to travel down the internal mammary artery, filling the arterioles about the apex of the heart. From the apex it has been observed to travel along the anterior descending and circumflex branches of the left coronary artery and to make its exit through cannulas placed in the origin of these vessels.

In regard to the angina pectoris of humans, we are of the opinion that this implantation should be of benefit, and that the implanted artery will form an anastomosis in human hearts much in the same way as it does in the animal. In fact, it is probable that the ischemia present in the human heart with coronary sclerosis will stimulate a collateral circulation. Therefore, the potential frequency of anastomotic formations in the hearts of humans with angina pectoris should be greater than that of normal hearts of animals. If, as is generally accepted, angina pectoris of man is caused by poor blood supply to the ventricles, then the introduction of a fresh source of systemic arterial blood through the internal mammary artery should be of considerable value in this condition.

The left internal mammary artery has been chosen as a source of collateral circulation for the following reasons: (1) it is easily accessible surgically, and is in proximity to the apex of the heart; (2) it arises close to the aorta and carries a high pressure; (3) it has numerous branches, which ensures a flow of blood through this vessel; (4) it does not supply blood to any vital organ; (5) it has proved to be surprisingly free of arteriosclerosis in human cases of coronary artery disease.[1]

The procedure of internal mammary implantation is, technically, comparatively simple and has many advantages. First, the short time during which the heart is disturbed: the actual implant of the artery into the heart can be easily performed within 2 to 3 minutes. Second, the artery is implanted into the ventricle through oblique wounds: it has been shown that oblique wounds of the heart tend to heal without a decrease in cardiac reserve (13, 15).

SUMMARY

Further studies of vascularization of the ventricular myocardium by left internal mammary artery implantation are reported.

Macroscopic and microscopic findings of animals developing collateral circulation are shown and described.

The frequency of anastomotic formation and the degree of protection afforded by these anastomoses are discussed.

An anastomosis has been shown to occur

[1]The results of dissection in the Department of Pathology, McGill University, will be reported in a subsequent publication.

between the internal mammary artery and the left ventricular circulation in from 50 to 73 per cent of the animals.

The degree of protection against coronary occlusion varies according to the size of the anastomotic channels. When there is a large anastomosis present, death and infarction from coronary occlusion do not occur.

Thrombosis of the implant limits the size of the anastomosis. When thrombosis occurred, in many instances small anastomoses developed through recanalized channels.

The operation is technically simple and appears not to damage the heart. Several advantages of the procedure and its potential value in certain human cases of coronary insufficiency are emphasized.

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THE ANATOMY OF THE PORTAL VEIN AND ITS TRIBUTARIES

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THE recent perfection of surgical procedures designed to ameliorate portal hypertension may be considered a practical consequence of the study of the anatomy of the portal vein. Various veins of the portal system have been joined surgically to veins of the inferior caval system in the hope that resultant shunting of blood would reduce portal tension to an extent sufficient to allow recession of the collateral circulation. Among the veins of the portal system utilized by various surgeons for this purpose have been the splenic (4, 5, 17, 18), the superior mesenteric (6, 27, 29), and the portal vein itself (2–4, 11, 14, 22, 26, 28, 30). This approach to the problem is meritorious in that it seeks to establish compensation for the results of portal hypertension rather than to treat locally the complications of an enlarged collateral circulation.

Standard texts and atlases of anatomy differ considerably in their depictions of the portal vein and its tributaries (8, 10, 12, 13, 19–21, 23–25). This is not remarkable in view of the inconstancy of veins in general, combined with the fact that the diagrams and sketches often represent a single dissection. The present study was undertaken with the intention of determining the approximate percentage incidence of major variations in the disposition of the portal vein and its tributaries.

MATERIAL AND METHOD

Material for the dissections consisted of upper abdominal organs removed at 92 necropsies. The specimens available for this study were exclusively from adult subjects on whom clinical study and postmortem examination revealed no evidence of portal hypertension, thrombosis or atresia of the splenic vein, hypoplasia of the portal vein, or previous surgical interference with portal flow. Through such exclusions it was planned to investigate and present the normal variations in anatomy of the portal vein.

To make these dissections possible, the spleen, pancreas, liver, gall bladder, stomach, and duodenum were removed en bloc and immersed in 3 per cent carbolic acid for 48 hours or more prior to dissection. The dissections were made primarily from the posterior aspects of these organs. After exposure and identification, each vein was laid open throughout its length to permit inspection of its interior surface.

Since the dissections were designed primarily to demonstrate the relationship between the portal vein and its tributaries, examination of the small veins and anastomotic arcs from which the major veins originate was not included; each vein entering the extrahepatic portal system was traced distally only to the extent necessary to determine the area or areas of its origin and thereby its identity. As the study did not include dissections of the intrahepatic branches of the portal vein, no information is offered concerning the termination of the cystic vein (except in certain cases which will be noted), the small veins accompanying the ligamentum teres hepatica and the ligamentum venosum, or the occasional accessory portal veins which have been recorded by Spalteholz.

METHOD OF PRESENTATION

It was both anticipated and demonstrated that the veins of the portal system, like those of the caval system, are disposed in widely varying patterns, particularly in respect to their anastomoses and points of termination.

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Abridgment of thesis submitted by Dr. Douglass to the Faculty of the Graduate School of the University of Minnesota in partial fulfillment of the requirements for the degree of Master of Science in Medicine.

TABLE I.—MEASUREMENTS OF VARIOUS VEINS IN CENTIMETERS

Vein	No. of dissections	Diameter		Length		Distance	
		Average	Range	Average	Range	Average	Range
Splenic	92	0.45	0.25–0.76	11.6*	3.6*–15.0*	2.8*	0.8–11.4*
Short gastric	82	0.07‖		3.2			
Mesenteric Inferior	92	0.32	0.13–0.45			1.2† 0.8‡	3.4 (max.)† 2.6 (max.)‡
Superior	92	0.83	0.51–1.08				
Gastroepiploic Left	92	0.19	0.13–0.38			3.5§	1.0–8.0§
Right	89	0.25	0.13–1.1				
Pancreatic veins	92	0.07‖					
Accessory pancreatic	29	0.13‖	0.19 (max.)				
Portal vein	92	0.89	0.64–1.21	6.4	4.8–8.8		
Pancreaticoduodenal Superior	92	0.13	0.07–0.25				
Inferior	92	0.13	0.07–0.38				
Coronary	90	0.25	0.13–0.38			6.8	2.4–11.5¶
Pyloric	76	0.07‖	0.03‖–0.19‖				

*Length after convergence of all trunks; distance from hilus to convergence of all trunks; see Fig. 2.
†Distance from superior mesenteric vein; Fig. 6a.
‡Distance from splenic vein; Fig. 6c.
§Distance from splenic hilus; for maximum see Fig. 4c.
‖Approximate.
¶Distance from porta hepatis.

For the sake of clarity in presentation, the various tributaries of the portal vein have been considered separately. In the case of each vein, minor variations were observed repeatedly. The major types and variations are represented by diagrammatic sketches, with numerical indications of the number of specimens in which each pattern was encountered, as well as its percentage incidence. The grouping of these variations has been entirely arbitrary, and each variation depicted represents in fact a compilation of a number of less significant variations. It was felt that the spatial relationships of structures in a large series of specimens could scarcely be presented without some such attempt at condensation of similarities. The principal configurations are designated "major types"; a second series of diagrams labeled "major variations" shows the most significant variations observed within the major types.

In occasional specimens we failed to identify certain veins. Such specimens were deducted from the total number exhibiting the vein in question before computation of percentages (exception: short gastric veins).

The caliber of the vein was recorded in centimeters and represented the widths of the collapsed veins. When the veins were distended with blood it is likely that the diameters were considerably greater than represented by the results of postmortem mensuration and the measurements are hereafter referred to as diameters. In most instances 3 figures are given: the average diameter of the veins measured, and the smallest and greatest diameters encountered. Data on the various veins are presented in Table I.

RESULTS

Major relationships of the portal system of veins. The proximal terminations of all the major veins of the extrahepatic portal system are shown in Figure 1, which is a compilation of the patterns most frequently encountered in the dissections of the 92 specimens. (In this and subsequent sketches the superior mesenteric vein is shortened somewhat, to allow depiction of its major tributaries.) The stomach and duodenum overlie these structures and the entire system is closely related spatially to the pancreas.

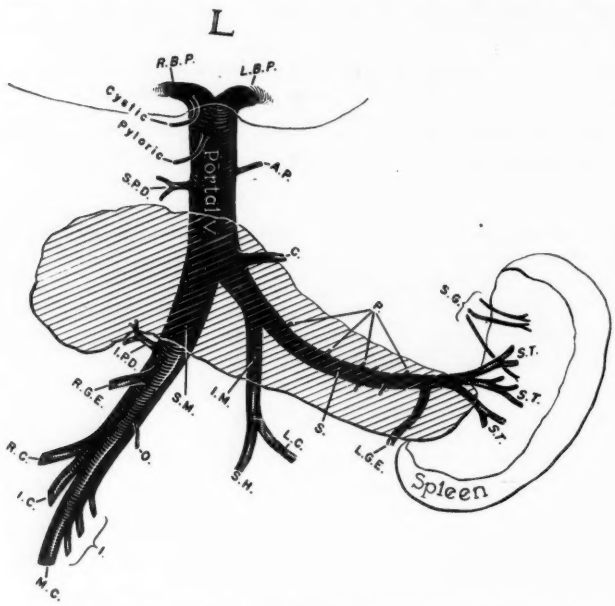

Fig. 1. The extrahepatic portal system of veins, anterior aspect. The termination of each vein is shown as it was encountered most frequently in the 92 dissections. The pancreas is represented by the shaded area. *A.P.*, accessory pancreatic vein; *C.*, coronary vein; *Cystic*, cystic vein; *I.*, intestinal veins; *I.C.*, ileocolic vein; *I.M.*, inferior mesenteric vein; *I.P.D.*, inferior pancreaticoduodenal vein; *L.*, liver; *L.B.P.*, left branch of portal vein; *L.C.*, left colic vein; *L.G.E.*, left gastroepiploic vein; *M.C.*, middle colic vein; *O.*, omental vein; *P.* pancreatic veins; *Pyloric*, pyloric vein; *R.C.*, right colic vein; *R.G.E.*, right gastroepiploic vein; *R.B.P.*, right branch of portal vein; *S.*, splenic vein; *S.G.*, short gastric veins; *S.H.*, superior hemorrhoidal vein; *S.M.*, superior mesenteric vein; *S.P.D.*, superior pancreaticoduodenal vein; *S.T.*, splenic trunks.

Brody and Young have reported gross anomalies of the portal system in which all or part of the pulmonary venous system terminated in the portal vein. No such extensive malformations were encountered in our 92 specimens.

In none of the specimens dissected were valves encountered in the veins of the portal system.

Splenic vein (*vena lienalis*). The splenic or lienal vein was formed near the splenic hilus by the convergence of a number of splenic trunks. These trunks emerged in fanlike arrangement from the crescentic hilus to join one another, according to highly variable patterns, behind and below the splenic artery at an average distance of 3.4 centimeters from the midpoint of the hilus. Frequently one or more of the trunks arose directly from the concave gastric surface of the organ or from either pole of the rounded eminence posterior to the hilar cleft. The splenic trunks were usually embedded in loose fat, which when removed revealed the presence of inconstant and variable cross-connections between them. One or more small veins often arose independently, to join one of the trunks before its juncture with other similar trunks.

The angle at which the trunks converged was highly variable, depending on the lengths of the several veins. Examples were noted in which a trunk arose at one or the other extremity of the hilus and coursed abruptly downward or upward to join a shorter mid-

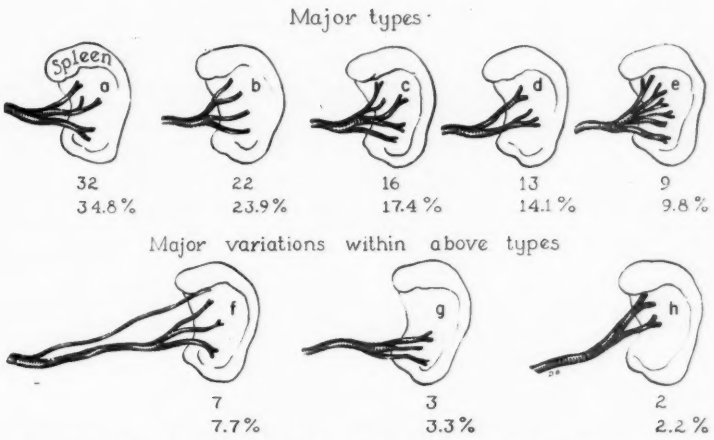

Fig. 2. a to h, The major types and variations of splenic vein in 92 dissections and the number of specimens in which each general pattern was observed.

hilar vein at approximately a right angle. The other extreme was encountered when one of the trunks was of disproportionate length and joined the splenic vein at an acute angle at a considerable distance from the hilus.

The diameters of the splenic trunks varied considerably (0.07 to 0.51 cm.) and it was of interest to note that in some instances the size of one or more of the trunks exceeded that of the splenic vein itself.

The splenic vein coursed below the splenic artery from left to right across the posterior aspect of the tail and body of the pancreas. Behind the neck of the pancreas it united at an angle approximating 90 degrees with the superior mesenteric vein. The average length of the splenic vein, measured from the splenic hilus to its juncture with the superior mesenteric vein, was found to be 15.0 centimeters. In no case was it found to be tortuous like the splenic artery. In approximately three-fourths of the specimens the splenic vein could be seen to lie in a distinct horizontal groove on the posterior surface of the pancreas. In a few instances the groove was completely obscured by overhanging pancreatic tissue, to the extent that considerable amounts of pancreatic tissue required removal before the splenic vein could be visualized. In most of the specimens the tail of the pancreas terminated several centimeters from the hilus of the spleen, leaving free the proximal portions of the splenic trunks and the first portion of the splenic vein. In some instances the tail of the pancreas was found to extend, with variable configuration, to the splenic hilus; in a few of the specimens the pancreas ended abruptly, its truncated end conforming with more or less accuracy to the concavity of the splenic hilus and embedding the splenic trunks in pancreatic tissue; in other cases the tail of the pancreas assumed a conical shape and deviated either anteriorly or inferiorly as it approached the hilus, its tip being entirely free of the hilar structures.

It will be noted in Figure 2a to h that the configuration most frequently encountered comprised three trunks but that the number of trunks ranged from two to six (exclusive of numerous short minor tributaries). In a few specimens the trunks arose exclusively from either the upper or lower portion of the hilar cleft, as indicated in Figure 2g and h. Seven of the specimens presented an excessively long trunk (Fig. 2f) which joined the splenic vein at a considerable distance from the confluence of the other trunks. Such elongated veins arose exclusively from the superior pole of the spleen in this group of specimens and in their course to the splenic vein were free of attachments to other structures. In the 7 instances these veins ranged

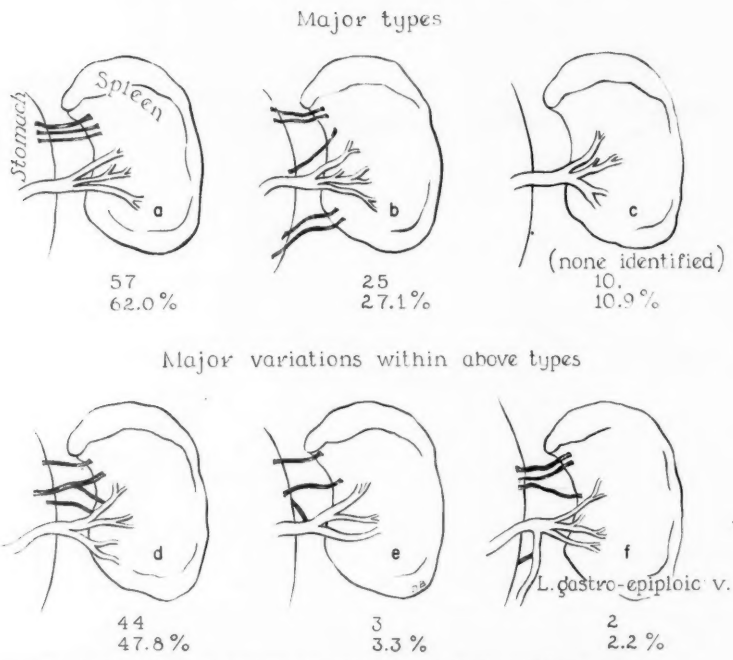

Fig. 3. a to f, The major types and variations of short gastric veins in 92 dissections and the number of specimens in which each general pattern was observed.

from 6.0 to 11.4 centimeters in length and 0.13 to 0.45 centimeter in diameter. Such veins might occasionally be of use in splenorenal anastomosis, especially when the point of confluence of the other splenic trunks is at a distance from the hilus, resulting, in effect, in shortening of the splenic vein.

Short gastric veins (*venae gastricae breves*). The short gastric veins drain blood from the left part of the greater curvature of the stomach, traverse the gastrosplenic ligament and empty into the splenic system of veins. They are said to be four or five in number (13). They are of very small caliber and difficult to identify in postmortem material, attempts at their isolation without injury being complicated by the tough, fibrous nature of the gastrosplenic ligament. As many as five such veins were identified in only a few of the specimens, and in 10 instances no short gastric veins could be identified.

The various dispositions of these veins are indicated in Figure 3. Short gastric veins terminating only in the upper posterior portion of the spleen or its hilus were identified in 57 of the dissections, whereas such terminations in the lower anterior portion were demonstrated in only 25. From this experience it is concluded that in the majority of instances the short gastric veins enter the superior portion of the spleen.

Many of the short gastric veins apparently emptied directly into the substance of the spleen, there being no demonstrable extrasplenic connection with the splenic trunks. Such connections as shown diagrammatically in Figure 3d, were observed in only 44 of the specimens dissected.

A single short gastric vein was found terminating in the splenic vein near its origin in 3 instances (Fig. 3e) and in the left gastroepiploic vein in 2 (Fig. 3f).

Left gastroepiploic vein (*vena gastroepiploica sinistra*). The left gastroepiploic vein arises from the greater curvature of the stomach, where it anastomoses freely with the right

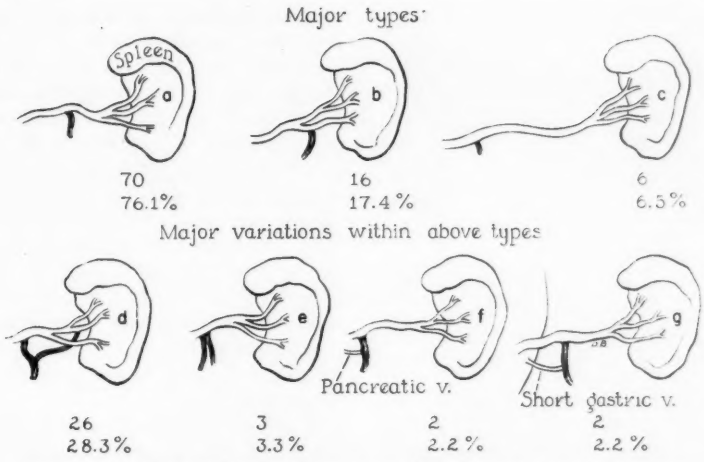

Fig. 4. a to g, The major types and variations of left gastroepiploic vein in 92 dissections and the number of specimens in which each general pattern was encountered.

gastroepiploic vein and receives tributaries from the greater omentum. It follows the greater curvature from its approximate midpoint, coursing from right to left. In 76.1 per cent of our specimens it entered the splenic vein near the origin of the latter. Its average postmortem diameter was 0.19 centimeter and in more than half the dissections it was found free of tributaries throughout its last 5 centimeters.

The most common termination of the left gastroepiploic vein was found to be the first portion of the splenic vein, within 2.0 centimeters of the formation of the latter (Fig. 4a). Second in frequency (17.4 per cent) was juncture with one of the splenic trunks (Fig. 4b). In 6 instances its termination was found to be more than 3 centimeters from the origin of the splenic vein; of this group (Fig. 4c) 1 dissection revealed the termination of the left gastroepiploic vein to be 8.0 centimeters from the splenic hilus.

Anastomotic connections with one or more of the splenic trunks were encountered, as indicated in Figure 4d. In a small number of cases the vein was found to be bifid. A single pancreatic vein and a single short gastric vein were found entering the left gastroepiploic vein near its termination in 2 instances each (Fig. 4f and g).

Pancreatic veins (*venae pancreaticae*). With the inconstant exception of its first few centimeters, the entire course of the splenic vein lies along the posterior aspect of the pancreas. It was found that numerous small veins drained the tail and body of the pancreas and entered the splenic vein at irregular intervals throughout its course. These veins seldom exceeded 0.13 centimeter in postmortem diameter and were usually only a few millimeters in length, as they emerged from the pancreatic lobules largely into the groove of the splenic vein, into which they emptied. In the 92 specimens as few as 3 and as many as 13 pancreatic veins were observed; the average number was 7; these terminated irregularly throughout the course of the splenic vein and occasionally in the superior segments of the superior and inferior mesenteric veins and the left gastroepiploic vein.

Only rarely did the pancreatic veins enter the exposed posterior surface of the splenic vein; in dissecting from the posterior approach they were most readily identified by laying the splenic vein open and noting their tiny orifices in the anterior wall of the latter.

In 29 of the specimens a prominent accessory pancreatic vein was observed. This vein received tributaries from the superior portion of the head of the pancreas or from islands of

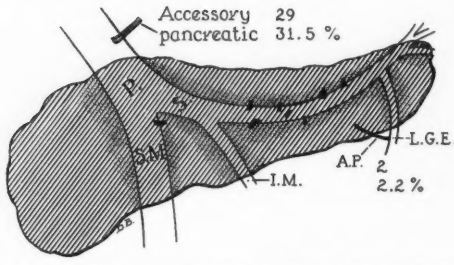

Fig. 5. The pancreatic veins, showing their distribution along the splenic vein (*S.*) and the percentage incidence (in the 92 dissections) of pancreatic veins emptying into the portal (*P.*) and left gastroepiploic vein (*L.G.E.*); *I.M.* inferior mesenteric; *A.P.*, accessory pancreatic.

aberrant pancreatic tissue interspersed between the layers of the lesser omentum. It was both longer and of larger caliber than the pancreatic veins which terminated in the splenic vein. In the specimens in which it was identified it terminated regularly in the superior aspect of the midportion of the portal vein. In 2 specimens a small accessory vein was found terminating in the left gastroepiploic vein.

The general configurations of the pancreatic veins are shown in Figure 5.

Inferior mesenteric vein (*vena mesenterica inferior*). The inferior mesenteric vein conveys blood to the portal system from the rectum, sigmoid, and descending colon. Its major tributaries are the superior hemorrhoidal vein, the sigmoid vein and the left colic vein. The former two veins usually unite to form a common ascending trunk before their juncture with the left colic vein. The vein so formed passes upward and medialward behind the body of the pancreas to terminate in the splenic or superior mesenteric vein.

The inferior mesenteric vein was identified with ease in all the dissections. Its tributaries were not available for examination, since removal of the specimens required severance of the vein below the pancreas. Usually it was found free of tributaries throughout the last 5 centimeters of its length.

As indicated in Figure 6 the proximal termination of the inferior mesenteric vein is variable, the commonest being in the splenic vein shortly before the junction of this with the superior mesenteric vein. In this group its greatest distance from the superior mesenteric vein was 3.4 centimeters. In 30 of the specimens the termination was in the portal vein in the angle formed by the union of the splenic and superior mesenteric veins, and in 27 specimens it was in the left wall of the superior mesenteric vein itself. In this group of specimens its greatest distance from the splenic vein was 2.6 centimeters.

In 3 instances the vein was represented by two trunks of approximately equal caliber; these were assumed to represent the superior hemorrhoidal and left colic veins. In 1 instance three trunks joined at the splenic vein; the third of these possibly represented a sigmoid vein.

Superior mesenteric vein (*vena mesenterica superior*). The superior mesenteric vein corresponds in distribution to the superior mesenteric artery, its chief tributaries from the intestine being the ileocolic, the right colic, the middle colic, and the intestinal veins. These trunks unite to form a single vein which ascends anterior to the third portion of the duodenum to unite with the splenic vein behind the pancreas. The juncture of these two vessels marks the origin of the portal vein.

The superior mesenteric vein was identified without difficulty in all the specimens. Without variation it was encountered as a single large trunk, relatively thick-walled in its proximal portion, joining the splenic vein in a broad confluence, its angle with the latter approximating 90 degrees. Due to the nature of the extirpated specimens the affluents from the intestine could not be differentiated, though the point of convergence of several larger trunks was frequently in evidence 7 to 12 centimeters below the origin of the portal vein. In the segment of the vein proximal to the convergence of the major branches, the right gastroepiploic vein usually entered anteriorly and the inferior pancreaticoduodenal vein terminated in the right lateral wall. Occasionally one or two omental veins were observed entering the superior mesenteric vein, usually in the vicinity of the termination of the right gastroepiploic vein.

The postmortem diameters of the superior mesenteric vein are indicated in Table I. The point at which measurements were taken was

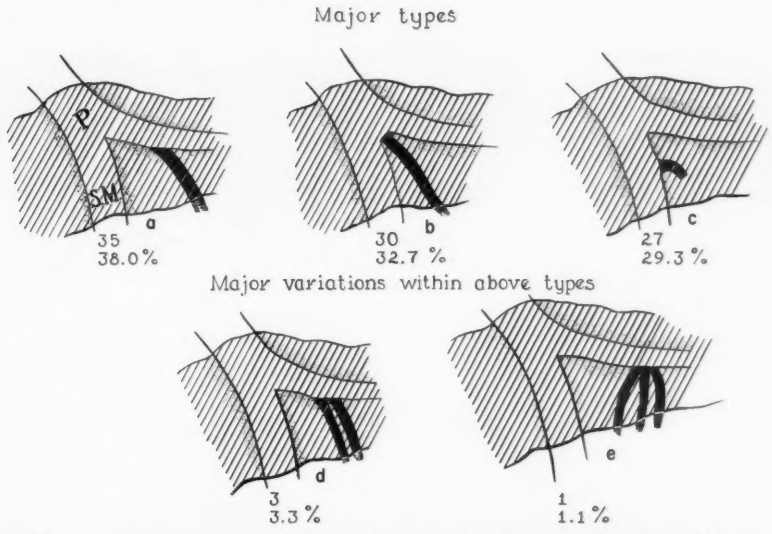

Fig. 6. a to e, The major types and variations of the inferior mesenteric vein and the number of specimens (of the 92 dissections) in which each general pattern was observed.

1.0 centimeter below the termination of the vein.

Portal vein (*vena portae*). The portal vein represents a confluence of veins from the unpaired abdominal viscera and conveys blood from these organs to the liver, within which it divides into a right and left branch.

The vein is formed behind the neck of the pancreas by convergence of the splenic and superior mesenteric veins. Thence it passes to the right and upward, behind the superior portion of the duodenum, to enter the liver at the right extremity of the porta hepatis. In its course it usually receives the superior pancreaticoduodenal vein, the pyloric vein, and in some instances the coronary vein and an accessory pancreatic vein. Its right branch is the usual site for termination of the cystic vein (13, 19, 20).

The portal vein was found regularly to be a broad, thick-walled trunk, loosely attached to its bed by thin fascial membranes. Its tributaries were dissected largely by tracing them distalward after visualizing their points of juncture with it.

Pancreaticoduodenal veins (*venae pancreaticoduodenales*). The pancreaticoduodenal veins receive tributaries from the head of the pancreas and adjacent segments of the duodenum. As indicated in Figure 7, they terminate regularly in the right wall of the portal or superior mesenteric vein, except in those instances in which the inferior pancreaticoduodenal vein terminates in the right gastroepiploic vein and thus discharges its blood into the anterior aspect of the superior mesenteric vein.

In 46 of the specimens two distinct pancreaticoduodenal veins were found, the upper terminating in the midportion of the portal vein and the lower in the right wall of the superior mesenteric vein. It appears suitable to designate these veins, respectively, the "superior" and "inferior" pancreaticoduodenal veins, in keeping with the designations of two of the pancreaticoduodenal arteries. The two veins were usually of comparable caliber, but the inferior vein exceeded the superior in length in most cases, and was free of tributaries throughout its final 2 or 3 centimeters, whereas the superior vein often emerged abruptly from the head of the pancreas just before entering the portal vein. Four of the specimens exhibited veins anastomosing the two pancreaticoduodenal veins.

In 35 of the specimens a single pancreaticoduodenal vein was found; its most frequent

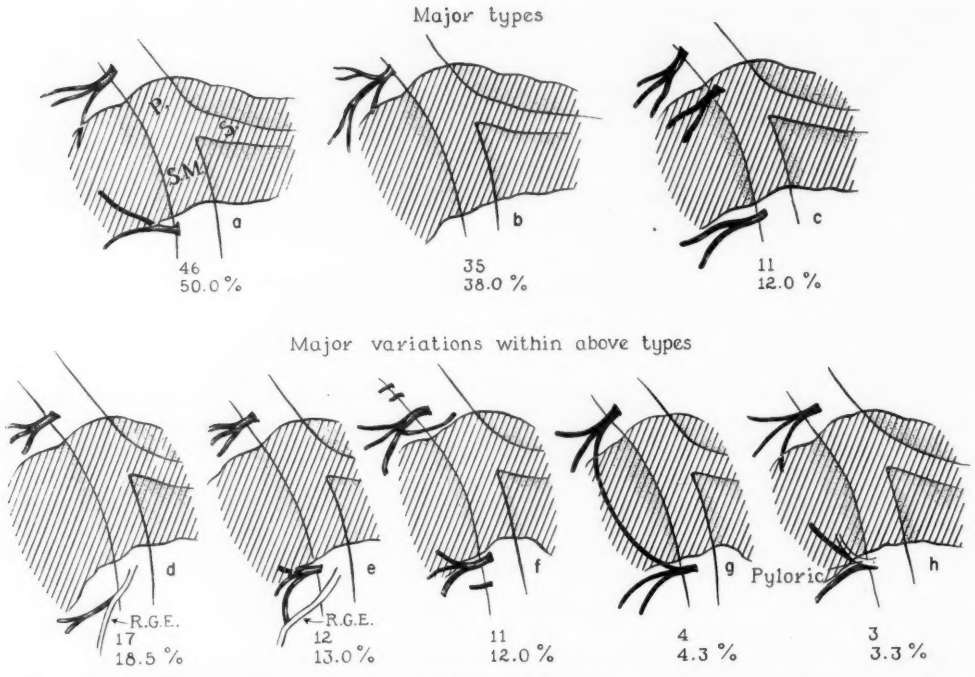

Fig. 7. a to h, The major types and variations of the pancreaticoduodenal veins and the number of specimens (of the 92 dissections) in which each general pattern was observed.

termination was at the inferior aspect of the portal vein. The diameter of the single vein approximated those of the separate veins outlined above, except in those cases in which a major bifurcation was evident in the terminal segment of the vein; in such cases the stem of the vein was considerably larger.

Three distinct pancreaticoduodenal veins of approximately equal caliber were found in 11 of the specimens. Multiple small separate veins, with and without proximal anastomosis with the major pancreaticoduodenal veins, were found in 11 instances also. Such veins ranged in number from one to four and terminated regularly in the right or right-anterior surface of the portal or superior mesenteric vein. In each of these cases the larger superior and inferior pancreaticoduodenal veins were identified.

The inferior pancreaticoduodenal vein joined the right gastroepiploic vein near its termination in 17 of the specimens. In 12 additional instances (Fig. 7e) these veins terminated separately but displayed a conspicuous proximal anastomosis.

In 3 instances (Fig. 7h) the pyloric vein terminated in the trunk of the inferior pancreaticoduodenal vein. No examples of termination of the pyloric vein in the superior pancreaticoduodenal vein were encountered, although the most common ending of the pyloric vein was high in the portal vein, considerably closer to the superior than the inferior pancreaticoduodenal vein.

Right gastroepiploic vein (*vena gastroepiploica dextra*). The right gastroepiploic vein anastomoses freely with the left gastroepiploic vein on the inferior aspect of the greater curvature of the stomach. It passes from left to right, leaves the stomach near the pylorus and then courses posteriorly, below and behind the pancreas, to terminate in the portal system. It receives one or more omental veins throughout its course.

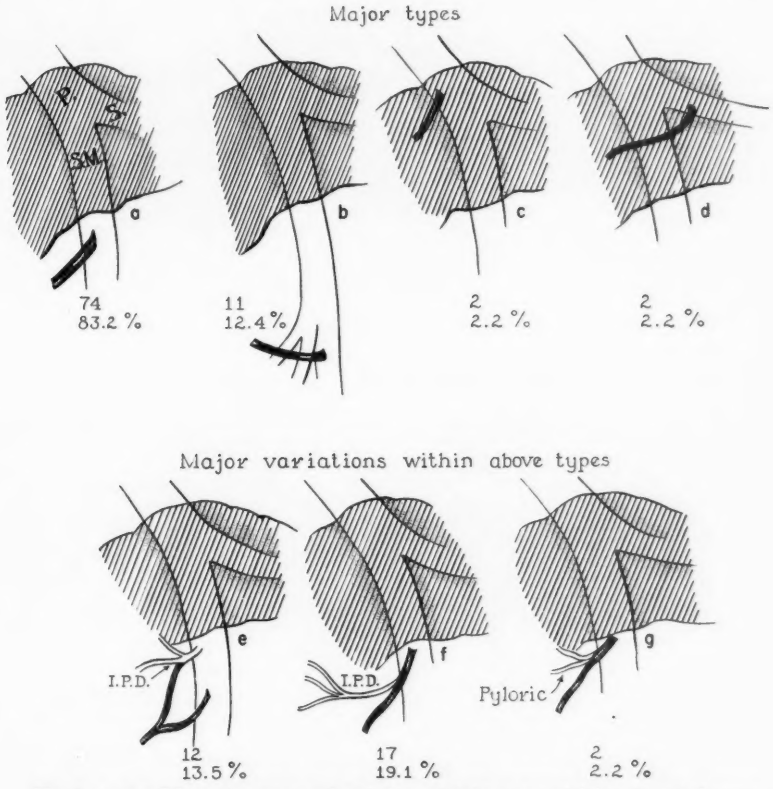

Fig. 8. a to g, The major types and variations of right gastroepiploic vein and the number of specimens (of 89 dissections) in which each general pattern was observed.

The average postmortem diameter of the right gastroepiploic vein was found to be 0.25 centimeter. In 1 specimen, in which the veins of the portal system were not otherwise remarkable, the vein was found to be hugely dilated (diameter 1.1 cm.) as it approached its termination; this diameter narrowed to 0.5 centimeter shortly before the vein joined the superior mesenteric vein.

The right gastroepiploic vein was identified in 89 of the 92 specimens. In 74 of these it terminated in the anterior wall of the superior mesenteric vein, most commonly at a distance of about 5 centimeters below the juncture of the latter with the splenic vein. In 11 instances it joined one of the tributaries of the superior mesenteric vein. The nature of the specimens made it impossible to identify this tributary; it has been reported (20), however, that the right gastroepiploic vein occasionally joins the middle colic vein, constituting a "gastrocolic vein." In 2 of the specimens the right gastroepiploic vein terminated anteriorly in the first portion of the portal vein and in 2 others it joined the base of the splenic vein.

The major variations encountered included proximal anastomosis with the inferior pancreaticoduodenal vein in 12 instances, reception of the same vein in 17 instances and reception of the pyloric vein in 2 instances (Fig. 8).

Coronary vein (*vena coronaria ventriculi*). The coronary vein of the stomach, known also as the "gastric" (19) or "left gastric vein," courses in the lesser omentum from right to left along the lesser curvature of the stomach.

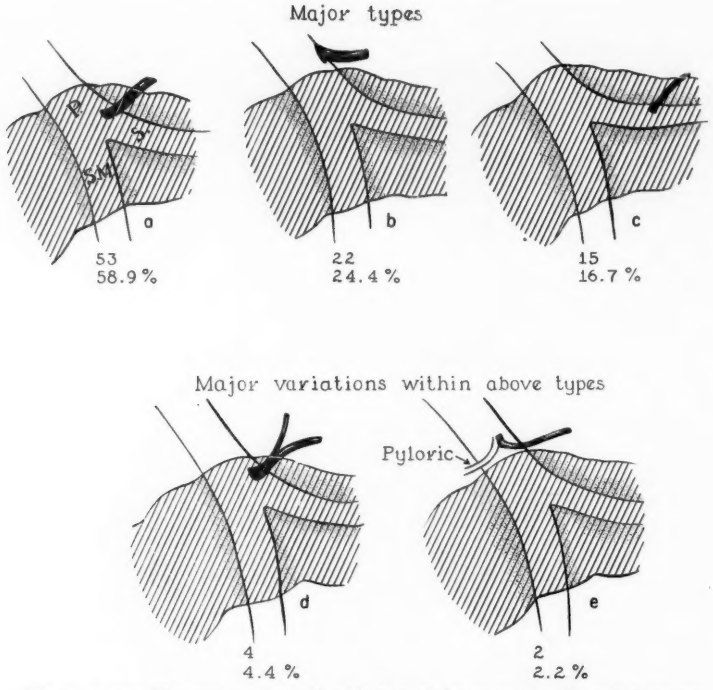

Fig. 9. a to e, The major types and variations of the coronary vein and the number of specimens (of 90 dissections) in which each general pattern was observed.

Near the esophagogastric junction it turns back upon itself and enters the portal system from above.

The coronary vein was identified in 90 of the 92 specimens. Generally, it was free of tributaries after its deflection from left to right. The length of this free terminal segment varied from 5.5 to 10.0 centimeters.

In 53 of the specimens the coronary vein terminated in the superior aspect of the juncture of the splenic and superior mesenteric veins (Fig. 9). In 22 it terminated in the portal vein proper, and in 15 in the splenic vein distal to its juncture with the superior mesenteric vein. Many gradations were found.

Major variations within the general types outlined were few in number and of infrequent occurrence. The vein was found to be bifid in 4 instances (Fig. 9d) and to join the smaller pyloric vein just before its termination in 2. A similar configuration was reported by Hochstetter.

In the standard textbooks of anatomy little mention is made of the relationship of the coronary vein to the pyloric vein. Morris indicated that the coronary vein usually ends in the portal vein "a little higher" than the pyloric vein. Our series of dissections shows that the coronary vein's termination is usually slightly below that of the pyloric vein.

In 2 instances the coronary vein could not be identified as it entered the portal system, though its cut end was found without difficulty. In these specimens insufficient hepatic tissue remained to permit investigation of the intrahepatic portal vein but it is believed that in these 2 specimens the coronary vein may have terminated within the liver, as observed by Hochstetter.

Pyloric vein (*vena pylorica*). The pyloric vein, known also as the "right gastric vein" (9), originates in the lower portion of the lesser curvature of the stomach and traverses the hepatogastric ligament to end in the portal

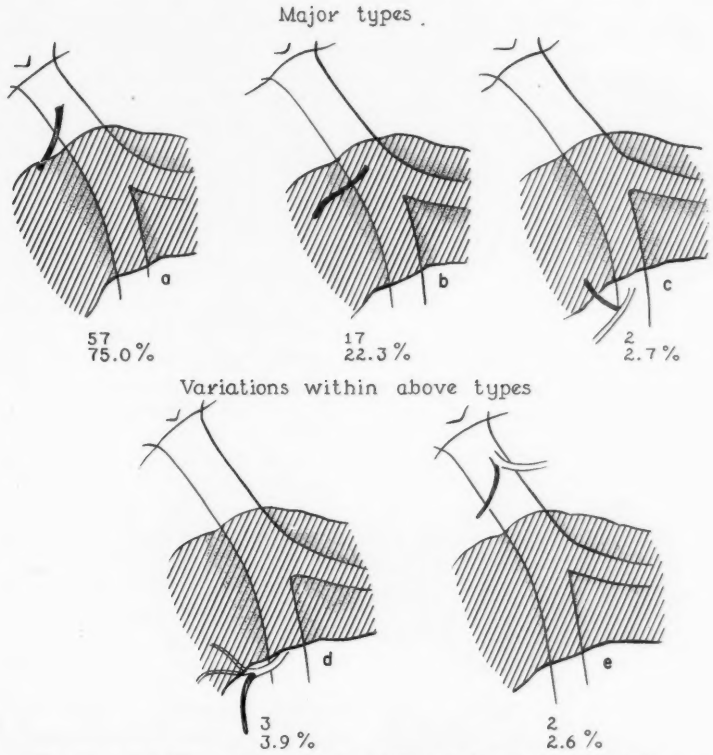

Fig. 10. a to e, The major types and variations of the pyloric vein and the number of specimens (of 76 dissections) in which each general pattern was observed.

system. It is very small and often difficult to identify. It is not to be confused with the "pyloric vein of Mayo."

The pyloric vein was identified in only 76 of the 92 specimens. Its principal configurations are indicated in Figure 10. In 57 of the specimens it was found to terminate in the anterior aspect of the portal vein, within 3.0 centimeters of its division into right and left branches. In many instances it was found that the apparent termination of the vein was not its actual one, since it exhibited investiture by the tunica adventitia for a distance of several millimeters before opening into the portal vein.

The pyloric vein was found to terminate in the region of the base of the superior mesenteric vein in 17 of the specimens (Fig. 10b) and in the proximal segment of the right gastroepiploic vein in 2 (Fig. 10c). Other infrequent variations included termination in the trunk of the inferior pancreaticoduodenal vein in 3 instances (Fig. 10d) and a common termination with the coronary vein in 2 instances (Fig. 10e).

The gastroduodenal vein depicted by Piersol was not identified in these dissections.

Cystic vein (*vena cystica*). The cystic vein conveys blood from the gall bladder to the portal system. Its length is short and it is said (9, 13, 19) to terminate usually in the right branch of the portal vein. Accessory cystic veins have been described (9) and the vein is said to consist occasionally of two separate trunks (20).

The gall bladder and major portion of the liver having been removed, the blocks of tissue available for this study did not permit

systematic investigation of the cystic vein. In 12 (13.0 per cent) of the specimens an unidentified orifice was encountered in the right inferoanterior aspect of the proximal segment of the portal vein. It is postulated that these orifices may have represented extrahepatic termination of the cystic vein.

COMMENT

In the normal subject, the pressure of blood in the portal system is 8 to 12 centimeters of water (1), approximating the tension of blood in the systemic veins. Therefore in the presence of portal hypertension one can reasonably anticipate reduction in tension if any portion of the portal flow can be diverted into the caval system. Moreover, the pressure differential can be expected to favor maintenance of patency at the site of anastomosis (4).

In the clinical evaluation of patients exhibiting evidence of portal hypertension, it is of primary importance to determine, when possible, whether the obstruction to portal flow is intrahepatic or extrahepatic. The obstruction is in all likelihood intrahepatic if there is clinical evidence of portal cirrhosis and laboratory indications of impaired liver function. The syndrome of gastrointestinal bleeding, splenic enlargement and thrombocytopenia, in the absence of demonstrable hepatic dysfunction, may indicate the presence of congestive splenomegaly due to extrahepatic obstruction to portal flow.

Among the recognized causes of extrahepatic portal obstruction are the following (28): (1) congenital atresia of the splenic or portal vein; (2) extension into the portal vein of the obliterative cavernomatous process which occurs normally at birth in the umbilical vein and ductus venosus; and (3) chronic progressive thrombosis. In this last group Whipple (29) has called attention to the etiologic role of pancreatitis and epigastric trauma; Kelsey, Robertson, and Giffin have added neoplastic lesions, surgical manipulation of abdominal organs, disease of the biliary tract, pylophlebitis, polycythemia vera, congestive heart failure, syphilis, hemolytic jaundice, duodenal ulcer, ingestion of phenol, omphalitis in infancy, subacute bacterial endocarditis, and atherosclerosis. Linton, Jones, and Volwiler considered it likely that fragmentation of thrombi may result in combined intrahepatic and extrahepatic obstruction to portal flow.

Thus it is known that, depending on the site of vascular obstruction, hypertension within the portal system may be localized or generalized. If the obstruction is intrahepatic, diversion of flow from the portal vein or any of its tributaries may be considered. If the obstruction is extrahepatic, veins suitable for use in the shunting procedures are only those whose junctions with the splenoportal vein are distal to the point of obstruction.

Blakemore and Lord and Blalock have emphasized the importance of locating accurately the site of extrahepatic obstruction to portal flow before attempting to divert a portion of the portal blood into the inferior caval system. They remarked that thrombotic obstructions are often difficult to palpate surgically and recommended localization of the block by determining the venous pressures in several tributaries of the portal vein. For example, in the presence of esophagogastric varices, normal pressure in the superior mesenteric vein or one of its branches and elevated pressure in the coronary vein indicate that the obstruction is probably in the splenic vein and that the coronary vein terminates in the splenic vein distal to the point of obstruction; in the presence of congestive splenomegaly, normal pressures in the superior mesenteric and coronary veins and elevated pressure in the splenic vein indicate that the obstruction is probably within the latter and that the coronary vein terminates proximal to the point of obstruction. Blakemore and Lord have also utilized 35 per cent diodrast as an aid in determining the site of termination of the coronary vein.

These same authors have called attention to the variable terminations of the coronary vein as depicted by six of the standard textbooks on anatomy, in four of which its termination is described as being in the proximal segment of the splenic vein. With reference to obstruction of the splenic vein owing to atresia or thrombosis, they indicated that esophageal varices are likely to develop when such obstructions occur proximal to the termination of the coronary vein. Our dissections indicate that localized obstruction of the splenic vein,

if of sufficient proximal extent, may affect coronary venous flow in approximately a sixth of the cases.

SUMMARY AND CONCLUSIONS

Measurements and configurations of the extrahepatic portal system of veins encountered on dissection of 92 specimens are presented.

The problem of surgical treatment of portal hypertension is considered and conclusions based on dissection of the portal system of veins in the 92 specimens are drawn as follows:

1. Measurable variations were encountered so commonly that in the case of certain veins of the portal system it appears quite impossible to propound a "normal" configuration. Anomalous patterns, therefore, must be considered only those which occur somewhat less frequently than others.

2. Preparatory to splenorenal anastomosis, mobilization of the splenic vein for a distance of 8 centimeters or more, as recommended by Blakemore and Lord, will be exceedingly difficult in those cases in which its posterior aspect is found completely covered by pancreatic tissue.

3. Mobilization of the splenic vein requires individual ligation of the pancreatic veins, which are short and often numerous.

4. When of sufficient diameter, the occasional excessively long splenic trunk may be considered to present an alternative to the splenic vein in the procedure of splenorenal anastomosis.

5. The short gastric veins are disposed in such fashion that they must be sacrificed during splenectomy.

6. Only occasionally is the termination of the left gastroepiploic vein sufficiently proximal so that its course would not suffer interruption by ligation of the splenic pedicle. When of sufficient diameter, its length and mobility suggest its possible utilization in anastomosis with the left renal vein.

7. An accessory pancreatic vein is found with sufficient frequency and in such position that care must be exercised in distinguishing it from the coronary vein. Generally it is of smaller caliber than the coronary vein.

8. Coronary venous flow will be obstructed by thrombosis of the splenic vein only in those cases in which the coronary vein terminates in the splenic vein (16.7 per cent of our specimens).

9. In manipulation of the portal vein, care must be exercised to protect or to ligate the superior pancreaticoduodenal vein, the pyloric vein, and, in some instances, the coronary, right gastroepiploic and accessory pancreatic veins.

10. The average length of the portal vein is 6.4 centimeters, somewhat shorter than usually stated (13, 19).

The multiplicity of variations encountered in these dissections emphasizes the importance of accurate surgical identification before the establishment of anastomoses involving tributaries of the portal vein. They make clear also the importance of visualizing the proximal termination of each vein under consideration for use in the shunting procedure.

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A STUDY OF THE SURGICAL SCRUB

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DURING recent years there has been considerable interest in devising a more effective and less time-consuming surgical scrub. A scrub may become more effective either as a result of more efficient removal of the bacteria from the cutaneous surface or by killing more of the bacteria. Price (10) introduced the term, degerming, to designate the combination of these two actions.

The mechanical removal of viable bacteria from the cutaneous surface is accomplished with the aid of soap or some other detergent. Materials which have specific germicidal action are either added to the detergent or used separately. Some years ago much emphasis was placed on the necessity of using ethyl alcohol as a germicide following the use of soap and water (5, 9, 11). With the development of new germicides, there has been a trend toward the substitution of these materials for the alcohol. It is not always clearly pointed out that the effectiveness of these new germicides is dependent upon their accumulative action. It was our purpose to re-examine some of the recently published surgical scrub techniques in light of work reported by us in our two previous papers (2, 3).

Many detergents other than soap have been developed in recent years and some of these have been used as cutaneous detergents (acidolate, dermolate, lowila, and *p*Hisoderm). These detergents have been reviewed by Lane and Blank. All of the commonly used cutaneous detergents belong to the general group of anionic surface active agents. Each of the cutaneous detergents belonging to this group effects some mechanical removal of bacteria from the cutaneous surface. None of these compounds by itself is a particularly good germicide.

The quaternary ammonium compounds (ceepryn, phemerol, and zephiran) belong to the general group of cationic surface active agents. These compounds are good germicides in vitro. Unfortunately they are not as effective germicides on the cutaneous surface as in the test tube (2). The mechanism of this loss in germicidal activity is now being studied by us.

Some of these quaternary ammonium compounds were originally thought to act as cutaneous detergents, but they do not effectively remove bacteria from the cutaneous surface (2, 7). The first of our papers (2) reviews the action of these compounds and shows that the normal negative charge on the cutaneous surface can be changed to positive by a quaternary ammonium compound, and that the positively charged surface attracts and holds the negatively charged bacteria but does not kill them. Subsequent to the use of these compounds an alkaline rinse will release many viable organisms from the surface.

In general, the higher the alkalinity of any scrubbing process, the higher will be the negative charge on the cutaneous surface and on the bacteria. This is the condition which will promote mechanical removal of bacteria from the cutaneous surface. Therefore, the alkaline detergents are more efficient than the acid detergents in mechanical cleansing.

Attempts to combine germicides, such as the phenols or the mercurials, with soap usually resulted in a loss in the activity of the germicide. In 1944, however, Traub, Newhall, and Fuller studied the action of soap containing hexachlorophene (G-11). This material was not inactivated by the soap. Mixtures of hexachlorophene with soap and other detergents were discussed in our second paper (3). In this paper it was concluded that:

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This is the third of a series of papers on the subject "Degerming the Cutaneous Surface," the first two of which have been accepted for publication in the *Journal of Investigative Dermatology*.

(1) hexachlorophene-detergent preparations, when used as a single short scrub, do not lower the bacterial populations of the skin any more than will a routine surgical scrub with soap and (2) hexachlorophene-detergent preparations have an accumulative effect, i.e., when used repeatedly for about 1 week they will appreciably lower the bacterial population of the skin.

Various workers (5, 9, 11) in this field have often concluded that alcohol is the most efficient agent for rapid degermation. This seems best expressed by Hatfield and Lockwood who state:

"We are inclined to recommend that principle reliance be placed on soap and water and ethyl alcohol in the preparation of the skin of operating personnel. . . . We urge, also, that in the use of alcohol and in other skin antiseptics the surgeon recognize the fundamental importance of the factor of time. Two minutes of continuous application of the alcohol to the skin is desirable, preferably accompanied by mechanical rubbing. The alcohol should be left to evaporate in order to further extend its action."

When ethyl alcohol became scarce during World War II, isopropyl alcohol was substituted and the latter has been found to be equally good for the degermation of the skin. Isopropyl alcohol has been reported to be an effective germicide over a wide range of concentrations (8, 13). Ethyl alcohol is efficient at a concentration of 70 per cent by weight but is said to lose its germicidal efficiency rapidly as its concentration increases or decreases (1). Neither ethyl nor isopropyl alcohol kills spores rapidly.

Some investigators have recommended elimination of alcohol from the technique of the surgical scrub (4, 12). This has often been suggested because it was thought that alcohol irritated the skin. In many hospitals, alcohol has been used customarily following a 10 minute soap and brush scrub. When the skin is irritated by such a scrub, it is felt that this irritation results from the following factors: (1) the physical trauma of the brush; (2) the hydration of the stratum corneum due to the *long* use of alkaline soap followed by the occlusion of rubber gloves; and (3) the removal of natural fats from the skin (a) by emulsification by the soap and water and (b) by solution by the alcohol. These factors can be minimized by shortening the soap and brush scrub, by using an acid dip following the alkaline scrub, and by adding an emollient to the alcohol in order to "lubricate" the skin. If the accumulative effect of a new germicide, such as hexachlorophene, is desired, this may be obtained by adding it to the alcohol and allowing the solution to evaporate from the hands.

It seems to us that elimination of alcohol from the scrub technique is not yet justified from the bacteriological point of view. In the following experiments we have verified the work of previous investigators who demonstrated the importance of a 2 minute alcohol immersion as part of the surgical scrub (5). We have done bacteriological studies of a scrubbing technique consisting of a short soap and brush scrub followed by a 2 minute immersion of the hands and arms in an isopropyl alcohol solution containing cetyl alcohol and hexachlorophene. We have compared this technique to the older and to the more recently recommended scrubs.

EXPERIMENTAL

In the bacteriological evaluation of any scrub, the method of determining the presence of bacteria on the cutaneous surface is of cardinal importance. Perhaps the most common method is the use of the sterile swab for transferring bacteria from the cutaneous surface to a culture medium. This method detects only those organisms which are transferred from the skin to the swab and subsequently leave the swab and go into the culture medium. It is not a quantitative method. There is also the skin biopsy method which is only practical for culturing wounds. This method determines the presence or absence of bacteria only on the small area of skin biopsied.

The details of the method we have used to evaluate the efficiency of a single scrub have been given in our second paper (3). Briefly, this modification of the Price technique includes washing the hands for 1½ minutes in each of 2 basins, each containing 2,000 milliliters of sterile water. The number of viable organisms removed in these basins is determined by the plate count method and thus there is obtained an indication of the number of organisms on the skin before the scrub. The

TABLE I.—SHOWING THE EFFECT OF LENGTHENING THE TIME OF IMMERSION IN ALCOHOL FOLLOWING A SOAP AND BRUSH SCRUB

Number of Viable Organisms per Milliliter of Basin Wash Water (2,000 ml. per basin)

Subject	Before the scrub			Scrub	After the scrub					Scrubbing index X/Y
	Basin 1 H_2O	Basin 2 H_2O	Total (1+2) Y		Basin 3 H_2O	Basin 4 H_2O	Basin 5 Soap+brush	Basin 6 H_2O	Total (3+4+5+6) X	
A	805	785	1590	I	264	193	222	221	900	56.6
B	2635	1091	3726		573	317	206	148	1244	33.4
C	6750	2150	8900		77	51	74	215	417	4.7
D	674	1076	1750		87	115	138	168	508	28.8
E	217	182	399		294	285	234	192	1005	250.1
F	2360	2670	5030		259	157	209	127	752	15.0
G	1465	1550	3015		310	337	125	57	829	27.6
A	404	457	861	II	21	42	19	33	115	13.3
B	471	324	795		9	9	9	12	39	4.9
C	995	483	1478		1	0	0	0	1	0.1
D	147	374	521		1	3	1	5	10	1.9
E	315	347	662		26	55	115	87	283	42.8
F	435	813	1248		3	10	40	5	58	4.6
G	550	609	1159		3	4	23	1	31	2.7

Scrub I: 10 minute scrub with soap and brush followed by a 15 second dip in 70 per cent isopropyl alcohol. Dry skin with a sterile towel.
Scrub II: 2 minute scrub with soap and brush followed by a 2 minute immersion in 70 per cent isopropyl alcohol. Skin allowed to dry by evaporation.

subject then performs a surgical scrub and after the scrub he washes in 4 basins, each of which contains 2,000 milliliters of sterile water. In the third of these 4 basins, sterile soap and a sterile scrub brush are used. The number of bacteria removed in these 4 basins is determined and the total number of organisms removed is taken as an indication of the size of the bacterial population after the scrub. This is an empirical method, but it was used by all of our subjects for the evaluation of all types of scrubs. We feel that it affords an adequate means for the comparison of the various scrubs. The *after count* divided by the *before count* we have called the *scrubbing index*. The most efficient scrub gives the lowest *after count* and the lowest *scrubbing index*.

First, we compared a 10 minute soap and brush scrub followed by a short (15 second) dip in isopropyl alcohol (70 per cent by volume) to a 2 minute soap and brush scrub followed by a 2 minute immersion in 70 per cent isopropyl alcohol. The hands and arms were rubbed during the 2 minute alcohol immersion and the alcohol subsequently was allowed to evaporate. The results of such a comparison on 7 subjects are shown in Table I. The subjects are members of our laboratory staff and not surgeons who might have had reduced bacterial counts from previous daily scrubs. Any 2 scrubs undertaken by any 1 subject are always separated by an interval of at least 1 week so the flora of the skin might return to normal following the first scrub. Much lower after counts and lower scrubbing indexes are obtained when the longer alcohol immersion is used. This degermation results from the efficient removal of bacteria by an alkaline detergent and the germicidal action of the alcohol.

In order to minimize the alcohol's drying effect (removal of natural fats) 0.5 per cent cetyl alcohol was added to the isopropyl alcohol. Cetyl alcohol is the principle ingredient of many commonly used cutaneous emollients. Hexachlorophene (0.1 per cent) was also added to the isopropyl alcohol. When a film of this solution is allowed to dry by evaporation, hexachlorophene is deposited on the skin and will lower the bacterial count on the skin when this solution is used repeatedly.

TABLE II.—SHOWING THE EFFECT OF AN ALCOHOLIC SOLUTION OF HEXACHLOROPHENE IN COMPARISON TO DETERGENT-HEXACHLOROPHENE PREPARATIONS

Number of Viable Organisms per Milliliter of Basin Wash Water (2,000 ml. per basin)

Subject	Before the scrub			Scrub	After the scrub					Scrubbing index X/Y
	Basin 1 H_2O	Basin 2 H_2O	Total (1+2) Y		Basin 3 H_2O	Basin 4 H_2O	Basin 5 Soap+ brush	Basin 6 H_2O	Total (3+4+ 5+6) X	
A	427	424	851		5	16	2	14	37	4.4
B	6770	1995	8765		4	3	3	2	12	0.1
C	2365	888	3253		1	4	0	3	8	0.3
D	216	253	469	I	3	5	7	0	15	3.2
E	386	822	1208		2	10	6	9	27	2.2
F	1173	866	2039		1	0	3	3	7	0.4
G	2040	956	2996		1	5	8	5	19	0.6
A	1145	1351	2496		1144	670	385	423	2622	105.0
B	1405	766	2171		146	101	144	41	432	19.9
C	955	539	1494		582	216	402	159	1359	91.0
D	630	420	1050	II	573	226	255	269	1323	126.0
E	46	54	100		195	205	91	263	754	754.0
F	745	440	1185		242	159	412	127	940	79.4
G	610	449	1059		894	778	193	223	2088	197.0
A	1270	406	1676		2	240	204	168	614	36.6
B	1023	431	1454		4	44	26	58	132	9.1
C	1218	646	1864		0	6	39	16	61	3.3
D	300	649	949	III	2	123	149	162	436	46.0
E	496	502	998		31	454	1021	382	1888	189.0
F	486	585	1071		2	119	145	74	340	31.8
G	463	362	825		1	91	257	188	537	65.0

Scrub I: 2 minute scrub with soap and brush followed by a 2 minute immersion in 0.1 per cent hexachlorophene and 0.5 per cent cetyl alcohol in 70 per cent isopropyl alcohol. Skin allowed to dry by evaporation.
Scrub II: 2 to 5 minute scrub with soap and 2 per cent hexachlorophene.
Scrub III: 2 to 5 minute scrub with pHisoderm and 3 per cent hexachlorophene, followed by a 1 minute dip in 0.1 per cent zephiran.

In Table II are shown the results of a 2 minute soap and brush scrub followed by a 2 minute immersion in the isopropyl alcohol solution of cetyl alcohol and hexachlorophene. The same 7 subjects as participated in the first experiment are used throughout these tests. The same low after counts and low scrubbing indexes are seen for the solution with added ingredients as were seen for the alcohol alone.

There are included in Table II, for comparative purposes, 2 sets of single scrubs on these same subjects using detergent-hexachlorophene preparations. In one scrub, each subject used a cake of soap containing 2 per cent hexachlorophene. He scrubbed each surface of his skin with 30 double strokes and his nails with 50 double strokes and then thoroughly rinsed his hands in running water. In another procedure, the skin was scrubbed the same way using pHisoderm with 3 per cent hexachlorophene instead of soap. This scrub was followed by a 60 second dip in 1 to 1,000 aqueous zephiran. The after counts and the scrubbing indexes for each are of the same high order as were obtained for the 10 minute soap scrub followed by the 15 second alcohol dip (as shown in Table I).

In a third type of experiment, a single subject scrubbed once daily for 5 successive days using a 2 minute soap and brush scrub followed by a 2 minute immersion in 70 per cent isopropyl alcohol. Each day before and after counts were obtained. After a lapse of 1 week, during which no scrubbing was done, this same

TABLE III.—SHOWING ACCUMULATIVE EFFECT OF HEXACHLOROPHENE WITH DAILY SCRUBS

Number of Viable Organisms per Milliliter of Basin Wash Water (2,000 ml. per basin)
(All scrubs were performed by the same subject)

Date	Before the scrub			Scrub	After the scrub					Scrubbing index X/Y
	Basin 1 H_2O	Basin 2 H_2O	Total (1+2) Y		Basin 3 H_2O	Basin 4 H_2O	Basin 5 Soap+ brush	Basin 6 H_2O	Total (3+4+ 5+6) X	
11/7	741	539	1280	I	6	2	1	5	14	1.1
11/8	234	62	296		0	5	0	0	5	1.7
11/9	410	56	466		21	3	9	24	57	12.3
11/10	199	38	237		2	2	6	18	28	11.8
11/11	534	117	651		0	4	4	4	12	1.8
11/28	5180	3520	8700	II	3	10	4	4	21	0.2
11/29	549	410	959		1	1	1	1	4	0.4
11/30	276	60	336		1	2	2	1	6	1.8
12/1	90	33	123		1	4	4	1	10	8.1
12/2	94	28	122		0	3	0	1	4	3.3

Scrub I: 2 minute scrub with soap and brush followed by 2 minute immersion in 70 per cent isopropyl alcohol. Skin allowed to dry by evaporation.
Scrub II: 2 minute scrub with soap and brush followed by 2 minute immersion in 0.1 per cent hexachlorophene and 0.5 per cent cetyl alcohol in 70 per cent isopropyl alcohol. Skin allowed to dry by evaporation.

subject performed an exactly similar daily scrub for 5 successive days, except that the solution of hexachlorophene and cetyl alcohol in isopropyl alcohol was used instead of plain isopropyl alcohol. It is interesting to observe in the data presented for this experiment in Table III that the before counts, during the week in which alcohol alone was used, dropped but did not drop progressively. When the alcohol solution containing hexachlorophene and cetyl alcohol was used, the before counts dropped progressively until, after 4 or 5 scrubs, the before count was less than 2 per cent of the original before count on the first day.

The final evaluation of a surgical scrub technique preferably should be made under actual operating room conditions. For this purpose, a number of surgeons washed in 2 basins previous to their surgical scrub. Before counts were obtained from these basins. Following the scrub, the surgeons put on their gloves and operated. The after counts were not determined until the end of the operation. Table IV shows the before and after counts and scrubbing indexes for 17 surgeons when using a standard 10 minute soap and brush scrub followed by a 15 to 60 second dip in 70 per cent isopropyl alcohol (Scrub I) and when using a 2 minute soap and brush scrub followed by a 2 minute immersion in the isopropyl alcohol solution of cetyl alcohol and hexachlorophene (Scrub II). For each surgeon, the after count is always low when Scrub II is used, independent of the length of the operation. In only 3 instances does a surgeon show a higher scrubbing index when he uses Scrub II than when he uses Scrub I.

In a total of 82 scrubs with the 2 minute alcohol immersion (Scrub II) carried out by 53 surgeons, the after counts ranged from 2 to 291 colonies per milliliter with an average of 50. In a total of 37 ten minute soap and brush scrubs followed by a brief alcohol dip (Scrub I) carried out by 23 surgeons, the after counts range from 12 to 4,025 with an average of 532. (In Table IV are shown the results of those scrubs by the 17 surgeons who performed both types of scrubs. The data from those surgeons who performed only one type of scrub are not shown.)

Two surgical services at the Massachusetts General Hospital have scrubbed according to the following directions from September 1, 1949 to May 1, 1950:

1. Wet hands and arms under running water and work up a lather with soap and brush.

2. Scrub each surface (fingers, hands, nails, arms to elbows) using 3 double strokes of the

TABLE IV.—SHOWING THE EFFICIENCY OF TWO TYPES OF SCRUBS UNDER ACTUAL OPERATING CONDITIONS

Surgeon	Scrub I				Scrub II			
	Length of operation (hours)	Colony count per ml.		Scrubbing index (X/Y)	Length of operation (hours)	Colony count per ml.		Scrubbing index (X/Y)
		Before scrub (Y)	After scrub (X)			Before scrub (Y)	After scrub (X)	
1	2¼	4,030	729	18.1	2¼	4,110	32	0.8
2	3	413	12	2.9	3	13,280	21	0.2
3	3	294	716	244.0	3	1,401	6	0.4
4	2 2½	984 939	520 462	52.9 49.2	2½	2,014	12	0.6
5	2	2,951	212	7.2	1 3	2,232 12,387	34 88	1.5 0.7
6	2 ¼	3,830 4,484	1,785 767	46.5 17.1	4	697	12	1.7
7	1½	674	101	15.0	3¼ 4¼	511 537	47 161	9.2 30.0
8	3	1,569	4,025	256.1	1 4	2,400 4,650	131 213	5.4 4.6
9	3½	850	112	13.2	3 3	822 6,465	291 112	35.4 1.7
10	1½	2,989	689	23.0	1 4	1,717 421	45 24	2.6 5.7
11	2½	197	83	42.1	1½ 3½	479 5,740	11 152	2.3 2.7
12	2	462	293	63.5	1¼ 1½	270 2,705	40 57	14.8 2.1
13	1½ 2	481 585	231 79	48.0 13.3	1½ 2 1½	1,531 3,058 14,810	30 20 12	2.0 0.7 0.1
14	2 2¼ 2½	1,635 3,880 400	143 770 461	8.7 19.8 115.0	4 2	1,480 1,210	2 24	0.1 1.9
15	3¼ 1	1,485 6,700	1,043 164	70.3 2.4	1½ 1 5	938 774 195	22 19 35	2.3 2.4 17.9
16	1¼ 2	596 499	951 33	159.5 6.6	2 2 1½	2,690 149 14,220	53 7 45	2.0 4.7 0.4
17	1½ 1 ½	1,455 1,895 715	52 217 89	3.6 11.5 12.4	3¼ 3 1 2 3 2½	1,065 1,124 716 3,220 1,000 206	24 32 16 22 9 7	2.3 2.8 2.2 0.7 0.9 3.4

Scrub I: 10 minute scrub with soap and brush followed by a 15 to 60 second dip in 70 per cent isopropyl alcohol. Skin dried with a sterile towel.
Scrub II: 2 minute scrub with soap and brush followed by 2 minute immersion in 0.1 per cent hexachlorophene and 0.5 per cent cetyl alcohol in 70 per cent isopropyl alcohol. Skin allowed to dry by evaporation.

brush on each surface. Rinse under running water. (Time—about 1 minute.)

3. Clean nails with an orangewood stick.

4. Scrub each surface again with 3 double strokes of the brush. (Time—about 1 minute.)

5. Rinse off soap completely and dry hands and arms with a towel.

6. Wet hands and arms thoroughly with the alcoholic solution of hexachlorophene and cetyl alcohol. (This may be done by immersing the hands and arms in the solution or by delivering it to the skin from a dispenser.)

7. Rub hands and arms for 2 full minutes being sure that the skin is kept wet with alcohol solution the entire time. (This may be accomplished by continuous immersion, repeated immersion, or repeated delivery of the solution from the dispenser.)

8. At the end of this 2 minute period, allow the hands and arms to dry by evaporation.

No instance of skin irritation which can be attributed to this scrub has been reported among the surgeons. Several have volunteered that the skin of their hands has been in better condition than during previous winters. The Massachusetts General Hospital is now adopting this procedure as its routine preoperative surgical scrub.

DISCUSSION

A surgical scrub should not be evaluated on the basis of the number of postoperative wound infections which develop from its use. Many factors other than the relative sterility of the surgeon's skin contribute to wound infections. Nevertheless, there can be no doubt of the importance of having as few bacteria on the surgeon's hands as possible, should his gloves be torn. Scrubbing techniques in which a minimum flora is reached only after repeated and exclusive use of the degerming substances have not seemed to us to be sufficient. The maintenance of a discipline of cleansing the hands with the same agent both within and outside the hospital is impractical.

There are further dangers inherent in the use of any scrub which depends upon an accumulative effect to obtain a minimum bacterial population. The surgeon using such a scrub has a false feeling of security. He is using a material which is known to reduce the bacterial population only after repeated application; and yet, unconsciously, he is likely to depend upon it for degerming his skin after but a single use. We do not yet know how quickly, following a single application, these materials degerm a skin which has been freshly contaminated. Price and Bonnett (11a) have expressed similar concern over the dependence on G-11 soap in the surgical scrub technique.

We wish to stress the need for a scrubbing routine which will leave a minimum bacterial population on the skin not only after repeated scrubbing but also *after only a single scrub*. We are recommending a scrub which first removes a maximum number of bacteria because an alkaline detergent is used, and then kills most of the remaining bacteria by a 2 minute immersion in isopropyl alcohol. Isopropyl alcohol maintains its germicidal efficiency even when diluted to a 50 per cent concentration. Hexachlorophene is added to the alcohol in order to maintain a minimum resident flora on the skin of those who scrub repeatedly. It is more efficient to apply the hexachlorophene to the skin with the alcohol than with the detergent, because, when applied with the detergent, much of the hexachlorophene is lost in the rinsing process.

No scrubbing technique is acceptable to the surgeon if it is irritating to the skin. Isopropyl alcohol tends to remove the natural fats from the skin. The addition of an emollient (cetyl alcohol) to the isopropyl alcohol, permits the deposition on the skin of a film of cetyl alcohol as the isopropyl alcohol evaporates. Since the melting point of cetyl alcohol is higher than the temperature of the skin, the resulting film does not feel greasy. This entire scrub produces a minimum of skin irritation because: (1) the period of scrubbing with a brush has been shortened; (2) the hydration of the stratum corneum is reduced because of the shorter exposure to the alkaline soap and the neutralization of any residual alkali by the acidity of the alcohol solution; (3) "dryness" of the skin is minimized by the addition of an emollient to the alcohol. Surgeons have found that when the skin is allowed to dry spontaneously after the immersion in the alcohol solution, the residual emollient leaves the skin sufficiently lubricated so that rubber gloves can be put on without the use of powder.

SUMMARY

Data are presented to show that detergent-hexachlorophene preparations do not yield *rapid* degermation of the skin. Under laboratory tests and actual operating conditions, *rapid* degermation of the skin is obtained by a technique consisting of a 2 minute soap and brush scrub, followed by a 2 minute immersion in a solution of 0.1 per cent hexachlorophene and 0.5 per cent cetyl alcohol in 70 per cent (by volume) of isopropyl alcohol. There is also an accumulative effect of the hexachlorophene after repeated scrubbing. The cetyl alcohol serves as an emollient for the surgeon's skin.

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UNHERALDED ACUTELY OBSTRUCTING CARCINOMA OF THE LEFT COLON

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CONTRARY to most standard teaching, cancer of the left colon can produce "sudden" catastrophic abdominal crises which are easily misdiagnosed and are often fatal.

In a survey of the autopsy material from the Mallory Institute of Pathology, Boston City Hospital, in a 12 year period (1936 to 1947 inclusive) we have reviewed 100 consecutive cases of carcinoma of the left colon (from the splenic flexure through the rectosigmoid) and have found 8 cases in which acute obstruction of the large bowel was the first evidence of any illness.

The survival time in most of these cases was unusually brief, chiefly because an early diagnosis of carcinoma of the large bowel with obstruction was not made. Several reasons for the variety of diagnoses were: (1) the lack of clinical evidence for a slowly developing obstruction and of previous obstructive symptoms; (2) a state of shock which obscured the true nature of the illness; (3) predominating symptoms of peritonitis; (4) a sudden onset of profuse diarrhea or vomiting or both suggesting infectious or toxic elements; and (5) misleading laboratory results in 1 case (an elevated urinary diastase test). These factors tended to suggest to the admitting physicians a multiplicity of diagnoses, all of which were in error. Because of this lack of appreciation of unheralded acute obstruction of the colon due to carcinoma, it is thought worth while to emphasize the occurrence of such a possibility in what we find to be 8 per cent of all carcinomas of the left colon coming to autopsy.

In most of the literature on this subject no attempt has been made to differentiate between a primary rapidly developing obstruction and an acute obstruction superimposed on one of a more chronic nature. Obviously the diagnosis in the latter condition is much simplified by previous obstructive signs and symptoms. It is unfortunate that some authors (5) in discussing this subject have used the terms "acute" and "complete" obstruction interchangeably, thus making interpretation of their cases difficult. The term "acute obstruction" in reality means the sudden development of an obstructive surgical emergency whether or not it be preceded by less dramatic symptoms. It will be seen that in many cases in which acute obstruction develops the obstruction is *not complete* because diarrhea, often of a considerable degree of severity, is associated with other evidence of obstruction.

Partial to complete obstruction of the colon due to primary colonic carcinoma is a relatively frequent occurrence. Obstruction in the left colon is 8 times as frequent as in the right (12) and has been found to occur in various series in from 35 to 60 per cent of the cases (2, 4). The average duration of symptoms before which the patient sought relief in these cases has been given as 9½ months (4) with a variation of from 3 weeks to 2 years. Miller, from the Johns Hopkins Hospital, noted unheralded acute obstruction 5 times in 128 colonic carcinomas and Reichel has observed it only 4 times in a series comprising 286 carcinomas with 144 complete obstructions. Rankin and Priestley and others state that in about 5 per cent of cases a sudden obstruction appears without any previous warning.

To illustrate several of the problems involved we present briefly the following cases:

CASE 1. A 42 year old housewife entered the Boston City Hospital on December 3, 1946 in a state of shock with nausea, vomiting, and diarrhea of 1½ days' duration. She was in perfect health until 36 hours before admission at which time she first noted generalized crampy abdominal pain which was soon followed by watery diarrhea and 1 hour later by nausea and vomiting. The pain disappeared but the

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other symptoms remained and she became very weak. She did not know of eating tainted food and no other member of her family had been ill. Similar but milder episodes had occurred 11 and 2 years prior to admission but no hospitalization was required. There were no previous operations.

Physical examination revealed a well developed and well nourished woman with no evidence of weight loss. The oral temperature was 101.4 degrees, the pulse 150, and respirations 38. The blood pressure was unobtainable. The patient was acutely ill, cyanotic, and breathing rapidly. She complained only of generalized weakness. The chest was clear and the heart was normal. The abdomen was soft, slightly tender with slight tympany; no masses were noted; peristalsis was diminished. Pelvic and rectal examinations were negative. The extremities were cold and cyanotic.

Laboratory data: The urines were normal. The hemoglobin was 66 per cent and the white blood count 8,000. The nonprotein nitrogen was 95 milligrams per cent, carbon dioxide combining power 33 per cent, fasting blood sugar 140 milligrams per cent and chlorides 61 milliequivalents per liter. Three stool specimens were guaiac negative. Stool cultures were negative for pathogens and enteric agglutinations were negative. Chest x-ray on December 5 was negative and an x-ray of the abdomen showed only marked dilatation of loops of small bowel over the entire abdomen.

Admission diagnoses were: Acute gastroenteritis, staphylococcal origin; cardiovascular collapse.

During the first 48 hours after admission the patient was given plentiful intravenous fluid therapy and 1 transfusion of whole blood. The blood pressure became obtainable and stabilized at 95/60. The patient continued to vomit and 30 hours after entry she was placed on gastric suction. At this time the abdomen was more tympanitic and distended. On the third hospital day the patient felt somewhat improved but she again had several profuse, watery bowel movements. Small bowel decompression was attempted with a Miller-Abbott tube but was unsuccessful. The patient died suddenly on the third hospital day, 60 hours after admission and 4 days after the onset of her illness.

Autopsy showed an annular constricting adenocarcinoma of the upper sigmoid with marked narrowing of the bowel lumen (less than 0.5 cm.), advanced large and small bowel obstruction, and metastatic implants on the cecal serosa.

CASE 2. A 69 year old man entered a surgical service of the Boston City Hospital on January 4, 1943 in a state of shock and with a history of being in good health until 5 hours prior to admission, at which time he was seized with crampy abdominal pain and began to vomit coffee-ground material. There was no history of peptic ulcer, cirrhosis of the liver, or bloody or tarry stools.

Physical examination showed the patient to be acutely ill and apprehensive. He was perspiring profusely, breathing rapidly, and had cold, clammy extremities. The temperature was 99.0 degrees, the pulse 140, and the respirations 40. The blood pressure was unobtainable. The chest was clear, the heart was normal, and there was no abdominal spasm or tenderness. The abdomen was distended; no masses were felt.

Laboratory data: The urine was negative and the hemoglobin was 80 per cent.

Admission diagnoses were: probable bleeding esophageal varices; shock.

The patient was given intravenous fluids and Wangensteen suction was applied with removal of copious amounts of fluid. The blood pressure did not rise and the patient expired 4 hours after admission to the hospital and 9 hours after the start of his acute illness.

Autopsy showed an annular constricting carcinoma of the splenic flexure with perforation and marked narrowing of the bowel lumen. There was advanced small and large bowel obstruction, fibrinopurulent peritonitis and metastatic tumor deposits in the lungs.

CASE 3. A 72 year old man was admitted to a surgical service of the Boston City Hospital on March 20, 1947 because of abdominal pain of 6 hours' duration. He stated that he had had intermittent abdominal pain for several years which was usually relieved by soda. Six hours prior to admission he developed severe abdominal pain in the lower epigastrium with radiation to the scrotum. The pain was followed by vomiting and these symptoms persisted until admission. He had been chronically constipated with no recent change in the bowel movements. The past history was incomplete because of the patient's condition.

Physical examination revealed an elderly, thin male who was cyanotic and in severe abdominal pain. The temperature was 96 degrees and the pulse was 100 and irregular. The blood pressure was 60/20. The lungs were clear and the heart sounds were distant. The abdomen showed generalized rigidity with tenderness most marked in the epigastrium. Peristalsis was absent. No masses were felt.

Laboratory data: The urine was negative, the hemoglobin 80 per cent and the white blood count 9,000.

Admission diagnoses were: probable perforated peptic ulcer; mesenteric thrombosis or dissecting aneurysm.

Clinical course: A scout film of the abdomen on admission revealed large amounts of free air beneath the diaphragm in the sitting position. Intravenous fluid and 2 whole blood transfusions were given. However, the patient did not rally; he remained in shock and expired 12 hours after admission and 18 hours after the acute onset of his illness.

Autopsy showed a perforated annular constricting adenocarcinoma of the lower descending colon with moderate constriction of the bowel lumen. There was mild large bowel obstruction present as well as fibrinopurulent peritonitis. There were no tumor metastases.

DISCUSSION

In adults suffering from acute intestinal obstruction Graham has found the lesion to be in the small bowel in 77 per cent of the cases and in the large bowel in the remaining 23 per cent. Burgess has noted 71.5 per cent and 28.5 per cent respectively in the small and large bowel. If a diagnosis of large bowel obstruction can be made, the possibility that the obstruction is due to a malignant tumor is very high. Brindley has quoted several authors who give percentages of 79, 80, and 90 per cent of all obstructing lesions of the large bowel as cancer.

Obstruction may develop in any portion of the colon and rectum. It can and does complicate carcinoma of the cecum, ascending colon, and rectum, but, as Pfeiffer and Martin have observed, in these sites other major symptoms and signs precede the actual obstruction and often make an earlier diagnosis possible. Hence it is usually in the transverse and descending colon and sigmoid that acute obstruction may develop as the first major symptom of a cancer. There is some contradiction to the above in the literature and the following statement is quoted from Graham: "... invariably patients who suffer an acute obstruction due to carcinoma of the colon had previously suffered for a varying length of time from chronic obstruction of the colon."

In the present series, with a knowledge of the pathology at hand, a reconstruction of the cases shows that there were extremely vague and nonspecific symptoms in 4 of the 8 cases. Other minimal earlier evidence of obstruction may have been present but such evidence was not elicited by the examiner taking a careful history. It might be pointed out that several of the patients were extremely ill upon entry to the hospital and it was impossible to obtain an extensive history from these persons.

The admitting diagnoses in our cases were extremely variable. They included large bowel obstruction of questionable etiology in only 1 case, acute gastroenteritis in 3 cases, acute pancreatitis in 2 cases and in addition mesenteric thrombosis, bleeding esophageal varices, incarcerated inguinal hernia with spontaneous reduction, perforated peptic ulcer, acute cholecystitis, and a variety of other diagnoses.

As mentioned previously, if the diagnosis of obstruction of the large bowel can be established the chances are 8 to 1 to 9 to 1 that the obstruction is due to a malignant growth. Among the possible causes of obstruction in the remaining 10 to 20 per cent of the cases (excluding strangulated external hernia which should be obvious) the most likely possibility is that the blockage is due to volvulus of a redundant sigmoid loop or diverticulitis with spasm. Infections (amebic, typhoid, etc.), benign tumors, adhesions, congenital bands, lymphomas, extrinsic tumors, endometriosis, "spastic ileus of the colon," and others rank far behind as precipitating causes.

That sudden obstruction of the left colon due to carcinoma may occur has been demonstrated. The factors contributing to sudden blockage of the bowel lumen are probably multiple and, as previously mentioned by many authors (6, 8, 10), they may represent any single factor or combination of the following factors: namely, (1) rapidly developing inflammatory edema; (2) impaction by solid feces; (3) kinking of the bowel with possible intussusception; (4) fatigue of the proximal colonic musculature; (5) narrower bowel diameter and lessened expansibility of the left colon as compared to the right; and (6) the pathologic characteristics of many growths in the left colon which are of the encircling stenotic "napkin ring" type. Cope has pointed out that when acute symptoms supervene in a case of cancer of the colon, it will usually be found that the ileocecal valve has lost its efficiency so that the obstructive pressure is forced back into the small intestine.

As stressed by Gruenfeld, the usual history in an unheralded suddenly developing obstruction is scant. If questions are pressed upon the patient he may vaguely recall some mild abdominal cramps, perhaps the necessity of a cathartic and may have even noted some loose stools or the presence of blood in the stools. However, it was only within a few hours, or 1 or 2 days previously, that he became concerned over the inability to move the bowels, or vomiting, diarrhea, abdominal fullness or pain. When diarrhea rather than obstructive signs predominate the picture may be quite confusing. Again, contrary to the usual state-

TABLE I.—PREDOMINATING SYMPTOMS

	No. of cases
Abdominal pain	8
Epigastric	1
Hypogastric	2
Generalized or unspecified	5
Nausea and vomiting	8
Diarrhea	3
Constipation (vague)	2

ments, some of our patients were in poor condition upon entry to the hospital because of the profuseness of diarrhea or vomiting or early perforation of the bowel with the appearance of local or generalized peritonitis.

The average age of the 8 patients in this series was 58.0 years, the youngest being 42 years and the oldest 72 years. There was a preponderance of males (7 to 1) in this small group.

The presenting symptoms in the 8 cases reviewed herein are listed in Table I. Abdominal pain was present in all cases (epigastric 1, hypogastric 2, generalized or unspecified 5), nausea and vomiting in all cases, diarrhea 3 cases, and constipation (vague in 2 cases, not mentioned in 1, and absent in 5 cases). Five persons were considered to be in the state of shock upon entry to the hospital or soon thereafter.

We again wish to stress that the duration of symptomatology prior to admission to the hospital was exceptionally brief and was one of the striking features of this series (Table II). In 1 case there were vague and mild abdominal pains for 4 weeks with a sudden onset of abdominal pain, vomiting, and diarrhea 8 hours before entry. In the remaining 7 cases symptoms were present for 36 hours or less and in 4 of these cases the duration was 6 hours or less. The length of survival in the hospital prior to death was not longer than 60 hours except in 1 case in which the patient survived for 26 days. Five persons survived less than 12 hours, emphasizing the severity of the situation. The total duration of life from the onset of symptoms is tabulated in Table III.

Physical examination upon entry to the hospital may reveal abdominal distention, usually of a marked degree and most prominent in the region of the cecum and ascending colon. Abdominal tenderness and rebound pain are present in varying degrees and peristalsis is variable; it may be hyperactive if obstruction is only partial and diarrhea is a feature of the illness. On the other hand, it may be hypoactive or absent in complete obstruction or when peritonitis has occurred. Aspiration of the stomach usually reveals clear contents of recently eaten foods. Most of the above findings were present in our cases during the course of the illness. Rectal examination may reveal the presence of a mass. A rectosigmoid tumor was said to be palpable by an observer in 1 of our cases. The stool guaiac was positive in 1 of the 5 cases in which that test was done in this series.

X-ray examination is often helpful in these cases. A scout film of the abdomen usually reveals the cecum and ascending colon and often the small intestine to be distended with gas. Free air may be present beneath the diaphragm in the upright position in cases of perforation. Sigmoidoscopy should be done and if it is normal a carefully administered barium enema may be very helpful in clarifying the site of the obstruction. Most of the patients described in this series were said to be either too ill to tolerate many diagnostic procedures or the suggestion of large bowel pathology was too vague to demand immediate survey of that organ.

It is our opinion that diagnostic procedures should be carried out despite the poor condition of the patient. Abdominal scout film (in the supine and upright positions), sigmoidoscopy, and a carefully administered barium enema will give valuable information and will form the basis of rational treatment. Without such measures many of these cases terminate fatally.

If the diagnosis of obstruction of the left colon has been established the treatment should consist of a transverse colostomy and use of antibiotics. Resection of the lesion can be performed after recovery from the initial abdominal crisis. It is true that some surgeons still prefer cecostomy to transverse colostomy in dealing with obstructing carcinoma of the left colon, but we have had much better results with simple loop transverse colostomy. We feel that the Devine type of colostomy should not be used for decompression in cases of obstruction of the left colon.

TABLE II.—DURATION OF SYMPTOMS PRIOR TO HOSPITAL ENTRY

Duration hours	No. of cases
0–6	4
6–12	1 (mild abdominal discomfort for 4 weeks)
12–24	2
24–36	1
Total	8

TABLE III.—TOTAL DURATION OF SYMPTOMS FROM THE ONSET TO DEATH

Duration hours	No. of cases
0–12	2
12–24	2
24–48	2
48–96	1
27 days	1
Total	8

In the 8 cases reviewed 2 patients were operated upon. In one of the cases closure without decompression was carried out, a mistaken diagnosis of pancreatitis having been made. In the other case decompression by ileostomy was done, a mistaken diagnosis of incarcerated inguinal hernia with spontaneous reduction having been made because of tenderness over the right inguinal area. Six patients were not operated upon.

The majority of tumors in this series were located in the sigmoid, there being 6 tumors in this portion of the colon, 2 of which were at the rectosigmoid junction. Of the remainder 1 was at the splenic flexure and 1 in the descending colon. Six of the carcinomas were of the annular constricting type and 2 extended as polypoid masses into the bowel lumen, but these also extensively infiltrated the adjacent bowel wall. Metastasis occurred in 4 of the 8 cases. Intestinal obstruction as seen at the autopsy table was moderate to marked in 7 cases and slight in 1 case. A measurement of the narrowed lumen of the bowel at the point of the tumor was made in all cases. The lumen was completely blocked in 1 case, markedly narrowed (0.5 to 1.0 cm.) in 6 cases, and moderately narrowed (1.5 cm.) in 1 case. It is remarkable that despite such degrees of narrowing in most cases so very few premonitory clinical signs and symptoms were present, illustrating again the treacherousness of such tumor growths in a portion of the large bowel which is much smaller in diameter than its proximal division, the right colon.

Peritonitis, whether frankly purulent or fibrinous and fibrinopurulent due to terminal passage of infection through a thinned and devitalized bowel wall, was present in all but 1 of the cases. Actual perforation at the tumor site or proximal to the obstruction was found in 4 cases. Three of these were obviously terminal perforations.

CONCLUSIONS

We have attempted to present the views and impressions of cases of suddenly obstructing carcinoma of the left colon as seen in a large general hospital. The diagnosis in all of these cases was obscure upon entry to the hospital and only suspected later in the illness in 2 instances. Death occurred rapidly in all but 1 of the cases. This series represents a somewhat select group inasmuch as the material was derived from the autopsy files and no consideration was given to cases in which recovery may have occurred after surgical alleviation of the obstruction. Our figure of 8 per cent of unheralded acute obstructions is somewhat higher but coincides fairly well with clinical observations which have been given by other authors.

It is pertinent to note that of 100 consecutive patients dying from carcinoma of the left colon 8 died with a stormy, rapidly developing, acute large bowel obstruction, and in most of these patients the actual diagnosis was not suspected before death.

SUMMARY

In a review of 100 consecutive autopsy cases of carcinoma of the left colon 8 per cent of the patients were found to have an acute unheralded intestinal obstruction as the first evidence of the disease process.

The history and symptomatology in these cases was often misleading and a variety of clinical diagnoses were entertained. Abdominal pain, nausea and vomiting, the early development of a state of shock, and occasionally profuse diarrhea were features of most of these cases.

The duration of symptomatology prior to admission to the hospital was exceptionally brief, being 36 hours or less in 7 cases and 6 hours or less in 4 of this group. Death occurred rapidly in all but 1 of the cases presented.

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A STUDY OF THE LIPIDS IN POSTPARTUM PLASMA

Its Use in Rheumatoid Arthritis

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THE investigation here reported was undertaken to ascertain whether or not there was any abnormality in the lipids of postpartum plasma.

It was first reported from this clinic (2) that a sustained remission could be produced in rheumatoid arthritis by the administration of suitable amounts of pooled postpartum plasma. A review of the literature failed to reveal any data on the use of postpartum plasma in rheumatoid arthritis. The remission was characterized by an amelioration of joint symptoms, an improved sense of well being, a brighter mental outlook, increased appetite, a gain in weight, restoration of the anemia and of the albumin-globulin ratio to normal. In general, the characteristic response was a striking clinical improvement. Over a period of 2 years there were no toxic effects and in 520 postpartum plasma transfusions there were no cases of homologous serum hepatitis. The longest remission to date following cessation of therapy was 14 months and the shortest was 3 weeks. During the investigation the author noted that the postpartum plasma had a greenish tint which was slightly opalescent and homogeneously distributed throughout the specimen. The mechanism of the beneficial effect of postpartum plasma in the treatment of rheumatoid arthritis has not yet been elucidated. Evidence exists to favor the view that this behavior is not due solely to steroidal factors.

CLINICAL MATERIAL

The material selected consisted of postpartum patients with no evidence of liver disease. All of the patients were on the wards of the obstetrical service of the Queens General Hospital. During the period of this study the patients were maintained on an ordinary diet.

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METHOD

Blood was obtained 48 to 72 hours after delivery and pooled so that each plasma specimen represented the blood of 10 mothers. Lipid estimations were determined according to the method which has been described by Bloor.

RESULTS

In Table I it is interesting to note that in the entire group of 8 pools representing 80 patients, the total plasma lipids varied from 363 to 525 milligrams and the average was 465 milligrams per cent. The fatty acids fluctuated from 277 to 409 milligrams and the average was 355 milligrams per cent. Amounts of phospholipids varied from 6.3 to 9.9 milligrams with an average of 8.2 milligrams per cent.

Table II shows that in 250 postpartum patients (48 to 72 hours after delivery) representing 25 pools, the total plasma cholesterol varied from 85 to 150 milligrams and the average was 119 milligrams per cent. The cholesterol esters varied from 15 to 110 milligrams with an average of 68 milligrams per cent. In pools 11 and 12 the cholesterol esters were too light to read.

TABLE I

Pool No.	Total lipids milligrams per cent (normal 500-700)	Fatty acids milligrams per cent (normal 200-420)	Phospholipids milligrams per cent (normal 7-14)
1	363	277	8.8
2	440	380	7.1
3	525	379	7.5
4	450	316	6.3
5	405	308	8.1
6	495	370	8.5
7	525	401	9.6
8	520	409	9.9
Average	465	355	8.2

TABLE II

Pool No.	Total cholesterol milligrams per cent (normal 160-230)	Cholesterol esters milligrams per cent (normal 100-150)
1	85	
2	90	
3	115	15
4	160	85
5	130	
6	90	30
7	140	92
8	120	97
9	125	80
10	140	110
11	100	Too light to read
12	105	Too light to read
13	120	
14	115	
15	110	
16	150	45
17	135	60
18	100	
19	125	
20	125	
21	120	
22	125	
23	150	
24	140	
25	110	
Average	119	68

DISCUSSION

From the evidence it appeared that the total lipids in postpartum plasma seldom exceeded the lower limit of normal. This decrease was also shared by the phospholipid fraction. The fatty acids, however, were within normal limits and were never elevated.

Unexpectedly, the albumin-globulin ratio was found to be inverted in all of the postpartum patients and the albumin levels were below normal (3).

One fact stands out in all the plasma determinations, namely that all of the cholesterol and cholesterol esters were well below the normal level.

In Table II the average total cholesterol never exceeded 120 milligrams and the cholesterol esters averaged 68 milligrams per cent.

CONCLUSIONS

In a group of 80 postpartum subjects the average total plasma lipids was 465 milligrams, the average for the fatty acids was 355 milligrams, and for the phospholipid fraction the average was 8.2 milligrams per cent.

In 250 postpartum patients the average total plasma cholesterol was 119 milligrams and the cholesterol esters were 68 milligrams per cent.

From these studies it is concluded that there is a decrease in the plasma cholesterol after delivery.

The possibility is presented that this decrease in cholesterol reflects the adrenocorticotropic (ACTH) activity in postpartum plasma.

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THE REPLACEMENT OF BLOOD VESSELS BY POLYTHENE TUBES

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THERE are times when the ability to replace a damaged blood vessel is of the greatest moment, particularly in the lower limbs where ligation of the main arteries has so often proved disastrous. The methods used, so far, have not been entirely satisfactory, and it therefore seemed that an experimental study of the problem might be of value.

Many methods have already been tried. Tuffier (15, 16) used paraffin lined silver tubes, but they usually filled with clot in 4 days or less, although some remained patent up to 10 days. Makins reported similar results in his own cases and in those of other surgeons. Murray and Janes (13) used glass tubes in dogs, but even with large doses of heparin these remained patent only up to 72 hours. Blakemore and associates used vitallium tubes in 15 dogs with only one success, in which the tube remained patent for 5 days.

Arterial grafts (Carrel, 2, 3; Gross and associates, 7) are clearly not suitable for general use. Vein grafts have been more successful (Murray, 12; Blakemore and associates), but the technique is by no means easy, whether suture or nonsuture methods are applied. Mustard and De Bakey and Simeone found that the method was not of much value in war wounds. And finally vein grafts cannot be used to replace arteries, for no big vein can reasonably be taken.

De Bakey and Simeone and Mustard also mention the use of plastic tubes in man, but it is not clear from their papers whether they did in fact use them. In dogs, Hufnagel has used specially polished methyl-methacrylate (perspex) tubes with considerable success. This substance is, however, hard and therefore troublesome to use. The chemical and physical properties of polyethylene (polythene), which are well known (Ingraham and associates), seem to be ideal for the replacement of blood vessels. Moreover, it is commercially available as extruded tubing in many sizes, is readily cut, can be bent to any required shape when heated, is nonirritant provided that the sample is not contaminated by plasticizers, is not wettable, and can be boiled.

Donovan has just described the use of polythene tubes in dogs. In 23 animals in which tubes of 5.5 to 7.5 millimeters' internal diameter were placed in the thoracic aorta, only one survived without a thrombus in the tube. Of 8 femoral arteries in 4 dogs in which tubes of 2.7 to 3.5 millimeters' internal diameter were placed, all thrombosed by the third day. Heparin was given to 2 more dogs, but clotting occurred on the fourth day.

ARTERIES

The following account is of the results in rabbits in which a length of thoracic aorta was replaced by polythene tubing. Despite the fact that the tubes were but 2.5 to 3 millimeters in internal diameter (except in 2 rabbits in which the tubes were 4 mm.), thrombosis occurred only in 8 of 20. In 5 of these the tubes were patent for 1½, 5, 6, 7, and 14 weeks, respectively, and in 1 the thrombus was due to errors in technique. Rabbits were used as the most readily available animal, and the thoracic aorta because it is the only reasonably sized vessel, because arteriograms are readily made, and because if clotting occurs in the tube it is at once obvious by weakness in the animal's hind legs.

Method. The rabbit is lightly anesthetized by intravenous injection of pentobarbitone (nembutal) and an intratracheal tube is passed blindly. For this purpose a No. 6 French rubber catheter is suitable, with the end cut obliquely: the animal is placed on its back, the tongue pulled out while the head is extended and the tube gently passed. The amount of

This work was begun as a MacKenzie MacKinnon and Beaverbrook research fellow at Bristol. The greater part of the experiments were, however, done at the Nuffield Institute for Medical Research, Oxford.

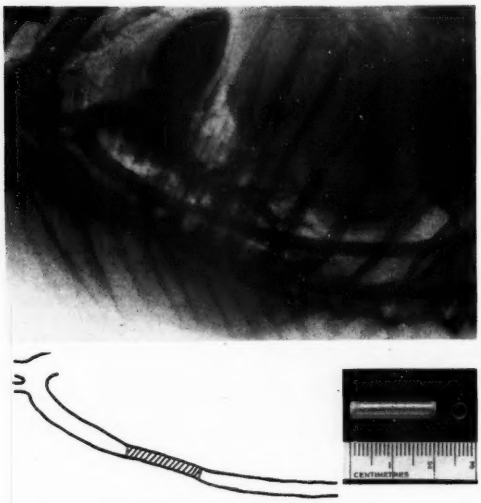

Fig. 1. Arteriogram of rabbit 13, taken at 6 weeks, using 2 cubic centimeters of thorotrast into the right ear vein, together with a tracing from the original film and a photograph of a tube of the same size as the one used. The animal is alive and well 4 months after its operation. The tube used was 21 millimeters long with an internal diameter of 3 millimeters and was bevelled.

extension is varied until the tube ceases to catch on the epiglottis and slips into the trachea—the rabbit at once coughs and the tube can be pushed in a few centimeters. The injection of pentobarbitone is continued until the breathing almost stops. Artificial respiration is then begun, a small physiological pump being used, at 28 strokes per minute; the stroke volume is adjusted according to the degree of chest expansion. The total amount of pentobarbitone needed is about 50 to 65 milligrams per kilogram.

The chest is then opened on the left side through the 5th, 6th or 7th interspace; the ribs are well separated and the stroke volume of the pump is adjusted so that the lungs just fail to collapse in expiration. The aorta is freed, the intercostal arteries tied between the sites chosen for the clamps and ligatures are passed under the vessel in such a position that they can be tied around the upper and lower ends of the tube. Small bulldog clamps are put as high and as low on the aorta as possible and the vessel is cut. (In the earliest experiments the aorta was not completely divided.) The tube is then introduced, with the greatest care not to injure or push up the intima, and is fixed by the ligatures already placed at each end. In Hufnagel's dogs, the ligatures sometimes cut through and secondary hemorrhage occurred; this did not happen with the polythene tubes in these rabbits, probably because a strong capsule forms round the tube (Figs. 2 and 5). This capsule was formed after 3 days in 2 animals, but in 1 animal was not very tough 12 days after operation.

If the aorta is clamped for more than 12 minutes there is danger that the animal will not recover from the anesthetic, or if it does that its hind legs will be paralyzed. (Some, however, will survive 15 to 20 minutes' occlusion.) The tube can usually be fixed in 5 to 7 minutes, and there seems to be no danger of a clot forming between its ends and the vessel, since the latter contracts down on to the tube.

The tubes used were 14 to 26 millimeters long with an internal diameter of 2.5 to 4.0 millimeters and a wall thickness of 0.5 millimeter. The outer edge was bevelled with a small file, after the size and length had been chosen, because it had been found in the earlier cases that the sharp edge made the introduction of the tube difficult. The operation (from incision to closure) takes about 1 hour.

Arteriograms (Figs. 1 and 2) were obtained on the anesthetized rabbits to see if clotting had occurred, if there were any changes in the aorta above or below the tube, particularly aneurysmal changes, or if the heart showed any obvious enlargement. Seventy per cent pyelosil, or thorotrast (which gives a better contrast) was used, 1 to 2 cubic centimeters being injected rapidly into the right ear vein (the left has a more circuitous course to the heart); as large a needle as possible was used, and serial roentgenograms were taken on a continuous roll of x-ray film at ½ second intervals. The faster the injection, the better the contrast in the pictures, and the fewer exposures necessary.

Results. In assessing the results the following points are relevant:

1. No anticoagulant or chemotherapy was used.

2. Apart from bevelling, the tube was not specially prepared.

3. Involving as it does, prolonged anesthesia, intrathoracic manipulations and obstruction of the blood supply to the lower part of the body, the operation is for any animal an especially severe one. The rabbit has a notoriously unstable cardiovascular system and these factors would be expected to produce a low blood pressure and predispose to thrombosis. The test is therefore as severe as can reasonably be devised.

4. It would seem desirable to use as large a tube as possible, but the larger tubes are much more difficult to introduce into the aorta, and the narrower ones remain patent even when they are a good deal smaller than the aorta (Fig. 2); indeed, the last 7 successful experiments were with tubes of 2.5 to 3 millimeters' internal diameter, whereas the internal diameter of the aorta is about 5 millimeters.

The results are briefly summarized in Table I.

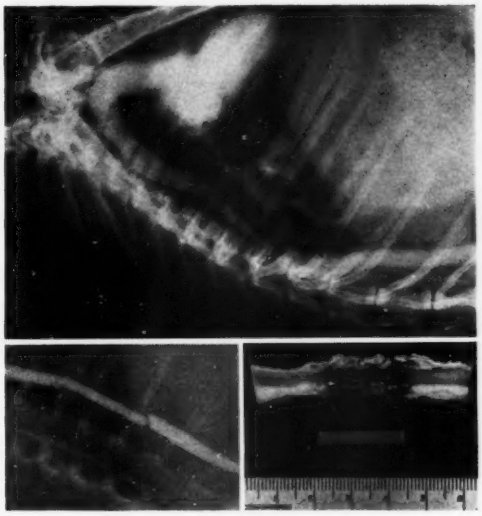

Fig. 2. Arteriograms of rabbit 18 taken at 4 weeks using 2 cubic centimeters of thorotrast into the right ear vein, and at 9 weeks by direct injection into the aorta immediately before death, and a photograph of the aorta and tube taken from the fixed postmortem specimen. This animal was killed because it developed a labyrinthitis. The rabbit is lying flexed in the first film and extended in the second, which accounts for the difference in direction of the aorta and tube in the two pictures. The aorta is small in the second film because of spasm of the vessel with handling and as a terminal phenomenon (the film was taken just before the heart ceased to beat). This spasm always occurs with handling of the aorta at operation, making difficult the introduction of the tube. The heart and aorta, both above and below the tube, are normal in appearance despite the fact that the tube is so much narrower than the vessel. The specimen shows a dark area, which is the "capsule" which surrounded the tube. The ligatures are clearly visible and the aorta, above and below the tube, is seen to be normal. The tube was 24 millimeters long with an internal diameter of 2.5 millimeters and was bevelled.

CASE REPORTS

Group 1. Failure to recover from the anesthetic (5 animals). In one rabbit (No. 2) the intima was lacerated and pushed up and clotting occurred at both ends of the tube. In 3 animals there was respiratory distress and they failed to recover from the anesthetic. In the fifth animal the operation seemed satisfactory, but the animal did not recover.

Group 2. Survival 1 to 12 days (4 animals). (a) This animal (No. 9) lived for 24 hours. There was slight weakness of the hind legs on the morning after operation and the animal died suddenly. Postmortem examination showed the tube partly blocked but no clot above or below. There was also a collapse of the left lung and free fluid in the chest.

(b) Two animals (Nos. 6 and 10) lived for 3 days. The first had slight weakness of the legs which became progressively worse. It was therefore killed and postmortem examination showed a clot starting at the lower end of the tube and partly occluding it. The second rabbit seemed quite well but died suddenly on the third day; there was no weakness of the legs. Postmortem examination showed the tube to be quite clear, but there was a clot about the size of a pin head on the aorta at the lower end of the tube. Death was due to bilateral collapse of the lungs and pleural effusions. In both a capsule had already formed round the tube.

(c) This animal (No. 16) seemed well for 12 days. It then became ill and was killed. The tube was partly blocked at the upper end by a small clot of fibrinous material. There was a well formed capsule round it, but this tore readily with handling.

Group 3. Survival for 1 to 6 months (7 animals). (a) Four animals (Nos. 19, 20, 7, and 12) lived normally for 5, 6, 7, and 14 weeks, respectively, and then died suddenly. In each case there was a thin membranous sheet arising from the aorta at the upper end of the tube and projecting into it (Fig. 5). In rabbits 12, 19, and 20, clot had filled the tube, inside this sheet: in rabbit 7 this had not occurred, but there was good deal of fluid in each side of the chest.

A firm capsule surrounded the tubes (see Figs. 2 and 5), which were bevelled.

(b) One animal (No. 18), in which an arteriogram at 4 weeks had shown the tube to be patent and the aorta normal, lived for 9 weeks and then developed an acute labyrinthitis. It was therefore killed with pentobarbitone. Immediately before death a second arteriogram was made by direct injection of thorotrast into the aorta. This showed the tube to be patent and the aorta normal, findings which were

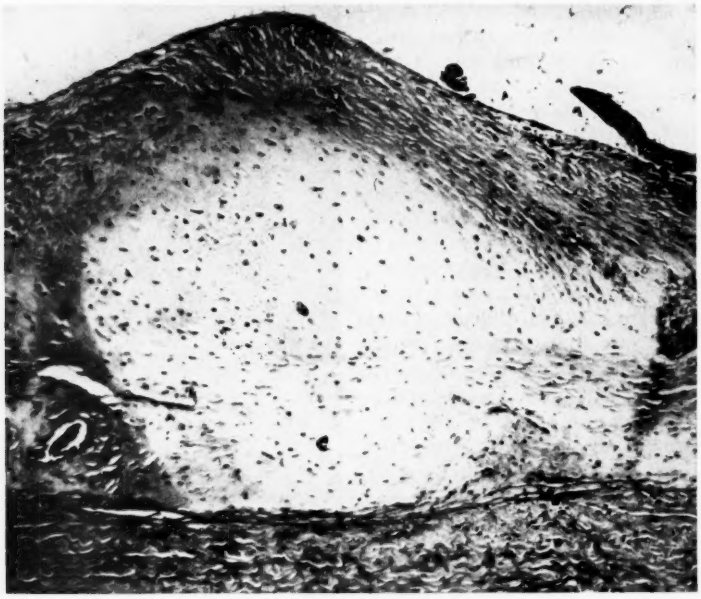

Fig. 3. Cartilaginous plaque in rabbit aorta involving intima and extending down as far as media. (Hematoxylin and eosin, × 80.)

confirmed at postmortem examination. The tube in this case was 24 millimeters long with an internal diameter of 2.5 millimeters and was bevelled (Fig. 2).

TABLE I.—A SUMMARY OF THE RESULTS OBTAINED

Survival	No. of animals	Rabbit No.	Thrombosis
Up to a few hours; did not recover from the anesthetic.	5	5, 11, 14, 17	None
		2	Clot, due to error in technique
1 to 12 days	4	9, 6, 16	The tube was partly occluded (1, 3, 12 days)
		10	The tube was clear but there was a minute clot on the vessel at the lower end of the tube (killed at 3 days)
1 to 6 months	7	3, 18	None (killed at 6 months and 9 weeks)
		1	The tube was patent but there was a small clot on the vessel at the lower end of the tube (died at 6 months)
		19, 20, 7, 12	The tube was occluded (died at 5, 6, 7, and 14 weeks, respectively)
Alive 3½ to 10½ months	4	4, 8, 13, 15	No evidence of thrombosis. Alive and well at time of writing

(c) This animal (No. 1) lived normally and in good health for 6 months and then died suddenly one night. The tube, which was 14 millimeters long with an internal diameter of 2.5 millimeters, was not bevelled and the aorta had not been cut right across when it was inserted. An arteriogram at 3 months showed that the tube was patent and that the heart and aorta were normal. Postmortem examination showed that the tube was patent; there was a small clot on the aorta at the lower end of the tube but this did not occlude it. Sections showed that there was a low grade infection around the tube.

(d) The tube in this rabbit (No. 3) was cut obliquely and bevelled, and was 15 millimeters long with an internal diameter of 4 millimeters. Arteriograms at 3 weeks and at 5 months showed the aorta and heart to be normal and unchanged, and the tube patent. The animal was killed at the end of 6 months in attempting to remove the tube and sew up the adventitia. The heart, aorta, and other vessels and the tube were normal macroscopically.

Group 4. Alive and well on February 28, 1950 (4 animals) (Table II).

Postmortem findings. The aorta above and below the tube seemed normal in all respects, even in those animals in which there was a thrombus at the junction of the tube with the aorta. A strong capsule was formed around

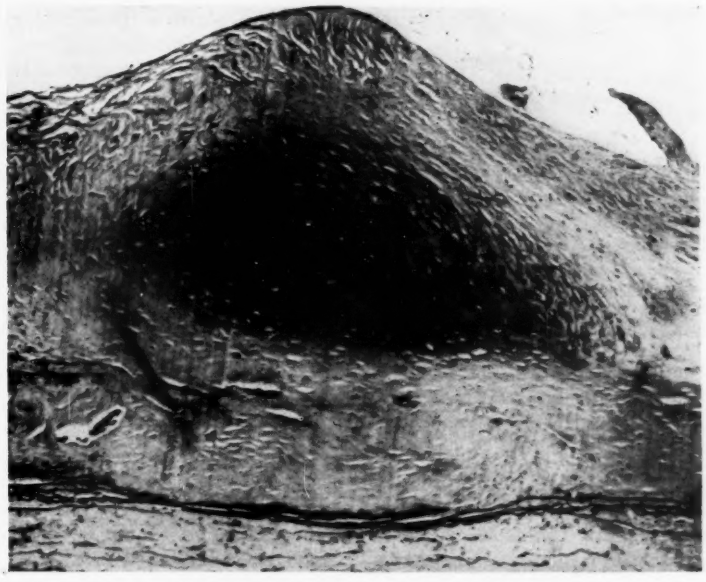

Fig. 4. A similar plaque showing metachromatic staining of cartilage and also showing elastica. (Orcein and toluidine blue, × 65.)

the tube, firmly attached to the aorta above and below (Figs. 2 and 5). This appeared very rapidly, within a few days (rabbits 6 and 10) and became strong with a smooth shining lining by the fifth week (rabbit 19), but not by the twelfth day (rabbit 16). In gross appearance it resembled the capsule formed round a tube when planted subcutaneously. There were some adhesions between the lung and this capsule. Three animals showed a thin membranous sheet projecting into the upper end of the tube which is described more fully in the histological report (Fig. 5).

Histological report by R. H. Cowdell, B.M., B.Ch. Oxford. Five portions of aorta (from rabbits 1, 3, 7, 19, 20) have been examined histologically. Each specimen (Figs. 2 and 5) was about 5 to 6 centimeters in length as received, and had a lumen of about 0.4 centimeter. In 4 of them there was a central portion about 1.5 centimeters in length where the wall appeared darker and slightly less smooth than elsewhere, while in the fifth the color was almost unchanged. At each end of this segment was a circular suture of thread running round in the adventitia and media. In 3 of the specimens a polythene tube just longer than the distance between the two sutures was received separately. The outer diameter of the tube was the same as that of the lumen, the inner some 0.1 centimeter narrower. In these 3 specimens there was a conspicuous annular swelling of the aortic lining which would be in apposition with each end of the tube. These thickened zones were smooth and rounded except in 1 instance in which a sheet-like tag of

TABLE II.—DETAILS OF THE 4 ANIMALS ALIVE ON MARCH 1, 1950

Date of operation	No. of rabbit	Details	Date of arteriogram	Arteriograms
a. 5, 4, 1949	4	The tube was bevelled and the aorta not completely divided	5, 25, 1949 9, 28, 1949 12, 12, 1949	Tube patent. Heart and aorta normal and unchanged
b. 10,14,1949	8	The tube was not bevelled. The aorta was completely divided	12, 12, 1949	Tube patent. Heart and aorta appeared normal
c. 11, 1, 1949	13	The tube was bevelled and the aorta completely divided	12, 12, 1949	Tube patent. Heart and aorta appeared normal (Fig. 1)
d. 11, 8, 1949	15	The tube was bevelled and the aorta completely divided	12, 12, 1949	Films unsatisfactory

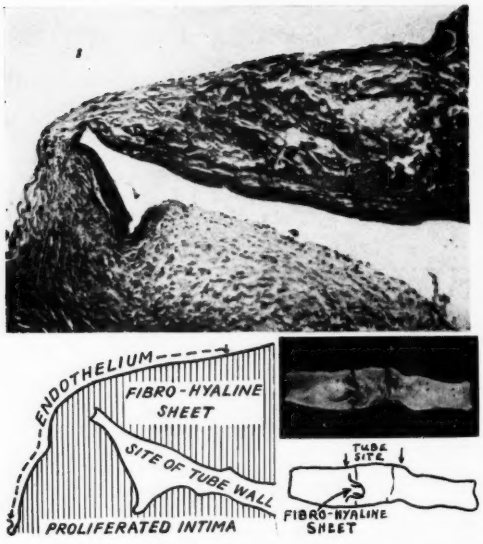

Fig. 5. Specimen from rabbit 7 showing the fibrohyaline sheet which arises from the intima and grows into the tube at its upper end: and a photomicrograph which shows the origin of this sheet from the intima and the endothelial lining near its base. (Masson's trichrome stain, × 55.)

white membrane hung down (Fig. 5). The lower end of this had been within the tube. In the 2 other specimens the tube was in situ and was filled by blood clot. In each of these there were similar intimal swellings, and attached to the one at the upper end of each tube was a similar membranous sheet which was prolonged to lie inside the tube, in one instance for three-quarters of its length, in contact with the inner aspect of the tube and surrounding the thrombus.

Microscopically (Figs. 3, 4, and 5) the changes varied only in degree, except in 1 case. The typical appearance was that the layers of aortic wall ceased abruptly between the sutures, and were replaced by a layer of dense collagenous tissue with longitudinally arranged fibers. This layer was of about the same thickness as, sometimes slightly thicker than, the aortic wall. It contained no elastica, and was not lined by intima. Adherent to the outer aspect in some instances were groups of striated muscle fibers, presumably from the diaphragm. The cut edge of the elastica showed no appreciable changes. The intima, however, showed proliferation to form a mound up to 0.15 centimeter in height consisting of material having a fibrocartilaginous structure, and staining metachromatically with with toluidine blue (Figs. 3 and 4). This corresponded with the swelling seen at each end of the tube in the gross specimens. In sections stained to show elastica two of the cartilage-like masses seemed to contain small fibrillary and rounded orcein-staining particles similar to those in areas where elastica is regenerating.

The membranous sheet seen in some instances (rabbits 7, 19, and 20) was of organized fibrohyaline tissue, covered for a short distance near its base by a single endothelium-like layer (Fig. 5). This arose from the apex of the proliferative intima.

The collagen of the new aortic wall close to the cut end of the elastica and at the level of the media just below the proliferated intima shows fibrinoid change, which continues to a lesser extent along the whole length outside the polythene tube.

The fifth specimen (rabbit 1 which died at 6 months) was similar to the others except that there was some chronic inflammatory infiltration of the fibrous wall outside the tube, with scattered groups of foreign-body giant cells.

Some areas, in parts of the aorta at a distance from the excised portion, showed all the morphological appearances of atheroma, with degenerative changes and groups of fat-containing histiocytes in the deeper intima and superficial media. These changes are a common spontaneous finding in the rabbit's aorta, and are easily induced by dietary means, which is one of the reasons why the rabbit has been considered an unsuitable animal for experimental study of arterial disease (Maegraith and Carleton).

Cartilaginous transformation in the aorta, usually reported as involving the superficial part of the media, is also of frequent occurrence, and is discussed by the same authors. Its situation in the present specimens suggests that it has occurred in response to the irritative effects produced by slight movements of the end of the polythene tubing, but in view of its reported spontaneous occurrence in other rabbits, no analogy can be drawn as regards the probable behavior of human vessels.

No tendency to formation of intima outside the polythene has been found, but the appearance of fibrohyaline sheets with a partial endothelial lining inside the tube suggests that it is possible that a complete internal endothelial layer might eventually form.

VEINS

The same method was used to replace lengths of the internal jugular vein; the tubes being 12 to 17 millimeters long with an internal diameter of 2.5 millimeters.

Ten veins in 6 rabbits were replaced. In the first 3 animals, no heparin was used and venograms were made on the twelfth, seventh, and third postoperative day, respectively. In the next 3, heparin was used, increasing the dosage from 25 milligrams per kilogram in 42 hours to 40 milligrams per kilogram in 22 hours, and venograms were made postoperatively at 42, 36, and 22 hours. In the fifth animal, one vein was replaced and the other internal jugular ligated to try to increase the blood flow in the intubated vein, and the tube itself was coated with silicone. In the sixth animal, heparin was begun before the tube was inserted.

In all 6 rabbits clotting had occurred by the time the venogram was made.

SUMMARY

1. A length of thoracic aorta in 20 rabbits was replaced by polythene tubing of 2.5 to 3 millimeters internal diameter (except in 2 in which it was 4 millimeters). In 13 of the animals, the tubes were patent at the time of death or are patent at the time of writing which is up to 10½ months after operation. In 8, thrombosis occurred, but in 5 of these the tubes were patent for 1½, 5, 6, 7, and 14 weeks, respectively, and in 1 thrombosis was caused by errors in technique.

2. The rabbits are divided into the following four groups:

a. Five rabbits did not recover from the anesthetic but in only 1 was death due to thrombosis in the tube (caused by technical errors).

b. Four animals lived up to 12 days. In 3 death was due to thrombosis in the tube, the fourth died from other causes.

c. Seven rabbits lived from 1 to 6 months. In 4, death was due to thrombosis. In the 3 others, the tube was patent at the time of death.

d. Four animals are alive and well at the time of writing with survival periods of 3½ to 10½ months.

3. Arteriograms in the living animals, and postmortem examinations on those which died showed that the aorta above and below the tube was normal.

4. A fibrous capsule forms rapidly round the tube and a fibrocartilaginous "buttress" forms at the junction of the tube and aorta. Histological examination in 3 cases showed in the inside of the tube, at the upper end, the beginning of an endothelial lining.

5. The replacement of 10 internal jugular veins in 6 rabbits was unsuccessful in all due to thrombosis in the tube. The use of heparin, and of a "silicone" lining and heparin, made no difference to the results.

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SMEAR PREPARATIONS IN THE DIAGNOSIS OF VULVAR CARCINOMA

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OUR group has described (1 to 7) the employment of genital smears in the study of uterine cancer. We have not stressed previously their use in the diagnosis of vulvar carcinoma.

Squamous cell carcinoma of the vulva comprises only a small percentage of the malignant tumors in our series. We do not therefore often have to identify this lesion by means of smears. The occasion arises more often in which cancer must be ruled out in the clinical evaluation of the much more common venereal lesions examined in the gynecologic and obstetric clinics.

The smear method of study can quickly provide the clinician with indications for subsequent diagnostic procedures. With the possible exception of the dark-field examination, smear interpretations can be made quicker than, or at least as quickly as, any of the other diagnostic methods by which the venereal etiology of vulvar lesions is established.

This paper contains pertinent data on patients who had squamous cell carcinoma of the vulva.

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METHODS AND MATERIALS

Genital smears were obtained, stained, and classified by methods described previously by us (2, 3).

It is difficult to obtain satisfactory smears from vulvar lesions by the aspiration technique. Smears made by drawing a microslide over the lesion have two primary faults. First, the cellular elements present are usually distorted by pressure in making the smear. Second, entire cells are seldom present in the exudate since the film usually is composed of the debris of necrosis. Therefore, we have found that scrapings made with a thin metal spatula, after the film has been removed from the lesion, result in the best smears.

Classification of smear types is made as follows:

Type I. Essentially normal epithelium.
Type II. Abnormal or atypical epithelium.
Type III. Intraepithelial carcinoma of the cervix. Questionable intraepithelial carcinoma of the cervix, or questionable malignancy.
Type IV. Cells thought to be malignant, few present.
Type V. Cells thought to be malignant, many present.

The smears were obtained on patients who came to the gynecologic and the obstetric clinics during the years from 1947 to 1949 inclusive.

The interpretation of the first smears obtained from a patient is used for statistical data. The original smears of the patients reported in this paper have been restudied for the purpose of analysis.

TABLE I.—DATA ON PATIENTS WITH CARCINOMA OF THE VULVA

Pt. No.	Age	Race	Marital status	Parity	Yrs. P-M*	Duration of lesion	Kind of lesion	Smear type, interpretation and malignant cell types				
									Original		Review	Cell types†
1	42	W	M	0–0–0	0‡	2 yrs.	Ulcerative, granular	V	Sq. cell ca., vulva	V	Sq. cell ca., vulva	B, C
2	64	W	M	0–0–0	15	3 yrs.	Ulcerative, indurated	IV	Sq. cell ca.	IV	Sq. cell ca., vulva	C, D
3	63	W	M	5–1–4	17	3 mos.	Fungating, ulcerative	IV	Sq. cell ca., vulva	V	Sq. cell ca., vulva	B, D, E
4	75	W	M	3–0–3	27	4 yrs.	Ulcerative	V	Sq. cell ca., vulva	II	Chronic inflam. process	
5	40	N	M	12–0–10	0‡	5 mos.	Granulating, ulcerative	V	Sq. cell ca., vulva	V	Sq. cell ca.	
6	64	W	M	6–0–6	20	3 yrs.	Ulcerative, indurated	IV	Sq. cell ca , vulva	V	Sq. cell ca.	
7	52	W	M	4–0–3	3	2 mos.	Ulcerative, indurated	III	? Vulvar malignancy	V	Sq. cell ca., vulva	A, C
8	66	W	Wid.	2–0–2	23	9 mos.	Papillary, ulcerative	II	Inflammatory reaction	IV	Sq. cell ca.	
9	67	W	S	0–0–0	24	3 mos.	Papillary, fungating, granulating	III	? Sq. cell ca.	V	Sq. cell ca., vulva	C, D
10	65	W	M	10–0–6	11	6 mos.	Granulating, indurated	V	Sq. cell ca., vulva	V	Sq. cell ca., vulva	B, C, E
11	72	W	M	0–0–0	32	4 mos.	Papillomatous, warty, dry	II	No malignant cells seen	II	No malignant cells seen	
12	36	W	S	0–0–0	0‡	4½ yrs.	Exophytic, friable, wart-like	IV	Sq. cell ca., vulva	IV	Sq. cell ca., vulva	C
13	66	W	Wid.	0–0–0	20	1 yr.	Reddened, infiltrated area	III	? Sq. cell ca., vulva	IV	Sq. cell ca., vulva	C
14	56	W	Wid.	8–0–6	13	2 mos.	Clean, epithelized	II	Inflammatory reaction	II	Chronic inflam. process	
15	68	N	M	4–2–1	? yrs.	6 mos.	Ulcerative	V	Sq. cell ca., vulva	V	Sq. cell ca.	
16	35	N	S	1–1–0	0‡	2 mos.	Granular	III	? Sq. cell ca.	V	Sq. cell ca., vulva	B, C, D, E
17	81	W	Wid.	10–1–5	30	2 yrs.	Ulcerative, necrotic	IV	Sq. cell ca.	IV	Sq. cell ca., vulva	B, C, E
18	54	N	Wid.	6–0–6	4	15 mos.	Ulcerative, friable. granulomatous	V	Sq. cell ca., vulva	V	Sq. cell ca., vulva	B, C, D

*Years postmenopausal. ‡Not postmenopausal. †Capital letters refer to cell types in Figure 1.

DATA

In the 3 years, 33,655 genital smears were made on 10,029 women.

Four hundred and thirty-four patients (4.3%) had cancer established by operative specimens. Eighteen patients (0.18%) had squamous cell carcinoma of the vulva. These cancers represent 4.1 per cent of the malignant lesions studied.

Table I presents pertinent data on the 18 patients with squamous cell carcinoma of the vulva.

Four patients were under 45 years of age; 3 were between 50 and 59 years of age; 11 (61.1%) were more than 60 years old.

Four patients were still having periodic uterine bleeding. The date of menopause in 1 patient was unknown. The duration of the postmenopausal period in the 13 remaining patients ranged from 3 to 32 years; average 18.38 years.

There were 14 white patients (77.8%) and 4 negresses (22.2%).

Three patients were single. Fifteen patients (83.3%) were, or had been, married.

Nulliparous women formed one-third of the patients, only 2 of whom were single. Eleven patients (61.1%) were multiparous; 4 multiparas, 7 grand-multiparas.

Location of lesions. The lesions involved the right labia in 11 patients (61.1%). The site in 3 patients was the left labia. The whole of the external genitalia was involved in 3 patients. The lesion was confined to the anterior fourchette in 1 patient.

Clinical impression. The clinical impression of the lesion in 15 patients was squamous cell carcinoma of the vulva or probable carcinoma of the vulva.

In patient 5, the impression was: "(1) granuloma inguinale; (2) carcinoma of the vulva; (3) lymphopathia venereum."

Patient 11 was thought to have leucoplacic vulvitis with kraurosis, but without definite leucoplacic formations, or carcinoma of the vulva.

The impression of the extensive lesion in patient 16 was "cellulitis of the vulva due to: (1) fusospirochetes; (2) lymphopathia venereum; (3) chanchroidal sensitivity. Carcinoma of the vulva to be ruled out."

The designation of malignant cells as of vulvar origin from smear preparations is based on the illustrations in the monograph of Papanicolaou and Traut, Plate H, Figures 19, 20, and 21. These authors infer that the cells illustrated usually can be associated with squamous cell carcinoma of the vulva. We concur.

Photomicrographs from our files have been chosen to illustrate these cell types. Therefore, the cell types of Papanicolaou and Traut are represented respectively by a, b, and c in Figure 1.

The 3 cell types are all basal in character, either round or oval. The nucleus of cell type a is less opaque than the others and has numerous chromatin granules and multiple prominent nucleoli. The perinuclear membrane is distinct. The nuclei in cell types a and c are irregular masses of chromatin material. However, the nucleus in cell type b may stain reddish, as shown in the monograph (8), or entirely black. The cytoplasm of cell type b stains red whereas the cytoplasm of cell types a and c stain green, green-blue or blue-gray. Cell type c may be larger than the other two but the nuclear-cytoplasmic ratio is approximately the same.

We believe, also, that there are additional cell types which are associated with carcinoma of the vulva more commonly and in greater numbers than in other squamous malignant lesions which we have studied.

One of these, cell type d, is a rather small basal cell with acidophilic cytoplasm and a large vesicular nucleus. The perinuclear membrane is extremely prominent. The chromatin forms a distinct open reticulum. There are usually multiple large nucleoli. There may be a faint orange coloration of the chromatin. As a rule the cell outlines are indistinct due to frayed edges. The nuclei, for the most part, are uniform in size and shape. The shape is round, sometimes ovoid.

The second cell, cell type e, is very large and flat. It resembles a highly cornified vaginal cell. The cytoplasm stains a bright orange-red. The nucleus is usually densely opaque. The nuclei are variable in size, irregular in outline and usually have jagged edges. The nucleus may be enlarged. There appears to be no marked variation in the nuclear-cytoplasmic ratio, when compared to a normal superficial vaginal cell, since the cell also is large. This cell probably represents a degenerating form in a well differentiated carcinoma. Such cells have been noted in smears of women who have had irradiation therapy for squamous cell carcinoma of the cervix. However, when these forms are present in large numbers we have found it advisable to consider vulvar carcinoma.

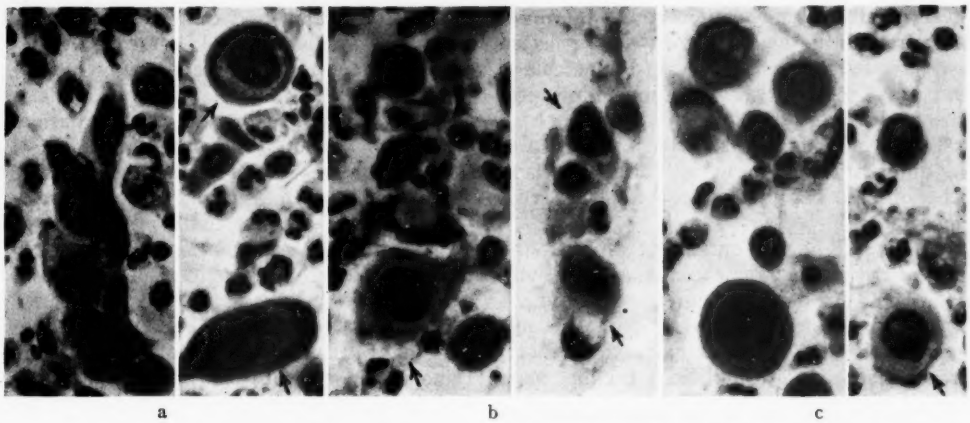
Evidence of metastases. Five patients (Nos. 2, 3, 6, 12, and 18) had metastases by tissue pathologic studies. Four patients were not investigated (Nos. 4, 7, 11, and 15). The lymph nodes studied in 9 patients did not show carcinoma.

DISCUSSION

Genital smears can be as valuable an aid in the diagnosis of vulvar as in other genital cancers. The percentage of error in underdiagnosis is approximately the same as the over-all underdiagnosis figure.

In the original interpretation of the smears from the patients with carcinoma of the vulva, three diagnoses were missed, an error of 16.7 per cent. In review, the smears of 2 patients still were classified as Type II. There were no malignant cells recognized. The lesions in these patients were dry and well epithelized or papillomatous and without exudate. These factors probably account for the lack of exfoliation of malignant cells in numbers sufficient for smear study. The smears on review of a third patient contained a few cancer cells that were found in clumps of debris and white blood cells. These were overlooked on the first examination of the smears. If this diagnosis had not been missed, the underdiagnosis percentage of error would have been 11.1 per cent which compares favorably with the overall underdiagnosis percentage of error, 10.4 per cent, for the 3 year period.

The review of smears was made by two of us who have studied together for 2½ years.



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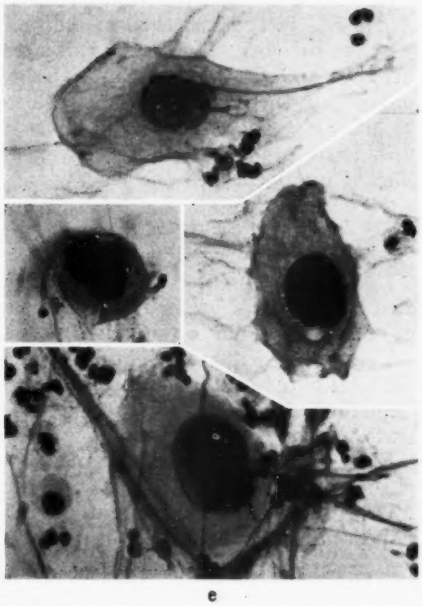

e

Fig. 1. Five cell types commonly seen in smear preparations of squamous called carcinoma of the vulva. Cell types a, b, and c are similar to those described by Papanicolaou and Traut (8), Plate H, Figures 19, 20, and 21.

The review diagnoses, arrived at independently, coincided in each case. At the time of rereading we did not know the identification of the smears nor the original interpretation of them.

The reclassification of a Type V smear as Type II can be explained on the basis of a faded stain. On review, no hyperchromatic nuclei were noted. Only an inflammatory reaction could be recognized.

We feel that the review changes of all the original Type III smears to Type IV and V were not due to retrospect but rather to conservatism on our part in expressing the degree

of atypical cell changes noted. At the onset of smear study, 3 years ago, we appreciated and have followed the advice of Papanicolaou and Traut to be conservative in the interpretation of smear cytology.

The smear method has been of value also in differentiating between carcinoma and other disease causing lesions of the external genitalia.

In several of the patients examined, the clinical impression was carcinoma of the vulva, with no strong suspicion of venereal etiology. When smear interpretations and subsequent biopsies proved negative for cancer, proper methods for establishing the diagnoses were instituted.

Some of the lesions reported herein had existed a relatively short time in the knowledge of the patients. Metastasis had already occurred in at least two patients. It should be obligatory, therefore, for the examiner to make smears, especially in the older age groups, from *any* vulvar lesion however insignificant in appearance and when a biopsy may not seem indicated.

SUMMARY

1. Data are presented on 18 patients, studied by the smear method, who had squamous celled carcinoma of the vulva.

2. These 18 patients represent 0.18 per cent of the total patients studied and 4.1 per cent of the malignancies which were found in these patients.

3. Eleven of the patients (61.1%) were more than 60 years of age.

4. Fourteen of the 18 patients (77.8%) were postmenopausal. In 13 of them, the postmenopausal period ranged from 3 to 32 years, an average of 18.38 years.

5. There were 14 white patients (77.8%) and 4 negresses (22.2%).

6. Eighty-three per cent of the patients were, or had been, married.

7. Six of the 18 women were nulliparous; 11 (61.1%) were multiparous.

8. Five cell types commonly found in smears from the vulvar carcinomas are illustrated. Three of these have been described and illustrated by Papanicolaou and Traut.

9. The genital smear method of studying malignant cells is of value not only in identifying carcinoma, but also in the differentiation, quickly, between cancer and vulvar lesions of venereal etiology.

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THE ENDOMETRIA ASSOCIATED WITH ECTOPIC PREGNANCY

A Study of 115 Cases

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HOW helpful is curettage in the consideration of a definite diagnosis in questionable cases of extrauterine pregnancy? It is the purpose of this study to determine whether examination of the endometrium contributes to the establishment of this diagnosis and to the recognition of the disease prior to rupture. Considerable reliance has always been placed on the gross appearance of the endometrium, and more especially the histological presence or absence of decidua. Failure to find decidua has been noted in the presence of an ectopic pregnancy subsequently confirmed at laparotomy. This poses several additional interesting questions. If decidua is not encountered at curettage, what is the nature of the uterine lining where the diagnosis of extrauterine pregnancy is later established? What is the incidence of the different types of endometria present? Finally, what may be the sequence of physiologic events which produced a specific endometrium?

HISTORY OF THE PROBLEM

The nature of the problem is emphasized by a historical survey of the literature. Boehmerus in 1752 first observed that a decidual lining was formed in the uterus of extrauterine gestation. He also stated that the organ enlarged somewhat, while becoming more vascular. William Hunter (1773) at the autopsy of a woman dying of tubal pregnancy noted that the uterus contained decidua. It was his impression that the decidua belonged to the uterus and was formed in it. He directed attention to the fact that in tubal pregnancy the organ was not enlarged presumably due to lack of a growing intrauterine conceptus. John Parry reviewed the subject in 1876 and was the first author to emphasize that decidua need not always be present in the uterus associated with an ectopic pregnancy. He interpreted the absence of uterine decidua to mean that the membrane had been previously expelled and not necessarily that it had never formed. Sampson (1914) was interested in the origin of the bleeding of extrauterine gestations. As a result of injection studies, he concluded that the bleeding was derived from the endometrium, was of venous rather than arterial origin, and a manifestation of involution. There has since been good evidence to dispute the venous origin of the endometrial bleeding (2). It is agreed, however, that uterine bleeding in ectopic pregnancy is endometrial in origin and not a retrograde backflow from an involved fallopian tube. Polak and Wolfe (1924) considered the majority of tubal pregnancies to be incomplete tubal abortions with bleeding persisting as long as the ovum was alive and attached to its tubal bed. They believed that if the ovum was dead, no decidual reaction would be found in the uterus. In this connection, Mall's classical work indicated that the embryo was usually either absent or dead when examined. Novak and Darner (1925), from a study of 21 cases of tubal pregnancy in which uterine mucosa was also available, concluded that the majority of such ectopic pregnancies are first observed after the death of the embryo at which time the endometrium has changed from its original decidual character, and that microscopic examination of the curettings is of little value.

Various authors have given the incidence of decidual findings as shown in Table I.

From The Pathological Laboratories of the Free Hospital for Women, Brookline, Mass., and the Boston Lying-in Hospital; and The Departments of Pathology and Obstetrics, Harvard Medical School, Boston, Mass.

TABLE I

	Total cases	Decidua	Per cent decidua	Per cent non-decidua
Sampson (1914)	25	5	20.0	80.0
Moritz and Douglass (1928)	53	8	15.9	84.1
Geist and Matus (1929)	39	23	58.9	41.1
Boerner (1931)	30	14	46.6	53.4
Siddall and Jarvis (1937)	38	22	57.8	42.2
Goldblatt and Schwartz (1940)	32	14	43.7	56.3
Aggregate totals	217	86	39.6	60.4

Siddall and Jarvis have a comparatively high incidence of 57.8 per cent of decidual findings and on this basis concluded that the study of curettings was a valuable diagnostic aid in ectopic pregnancy. Moritz and Douglass questioned whether there was initially a complete decidual formation of the endometrium in every case of tubal pregnancy. They had encountered several cases of early tubal pregnancy in which uterine bleeding was absent and the uterine lining failed to reveal decidua. Goldblatt and Schwartz sought to correlate the phase of the endometrium, the Friedman test, and the state of viability of fetal trophoblastic elements and villi. The presence or absence of uterine decidua was probably related to the amount and duration of bleeding. It was also their impression that the finding of decidua was a function of the extent of viability of the fetal components of conception. This review of previously reported studies (each composed of a relatively small number of cases) emphasizes the apparent discrepancy in the incidence and value of decidual findings in ectopic pregnancy.

MATERIAL STUDIED AND FINDINGS

All the cases of ectopic pregnancy at the Boston Lying-in Hospital and the Free Hospital for Women in the 10 year interval from 1938 to 1947 inclusive were reviewed. Of these 175 cases, the endometria of 115 were available for study. The diagnosis of pregnancy was verified in each instance by the finding of some ovular component, either a villus, ghost villus, or a portion of trophoblast in an ectopic site.

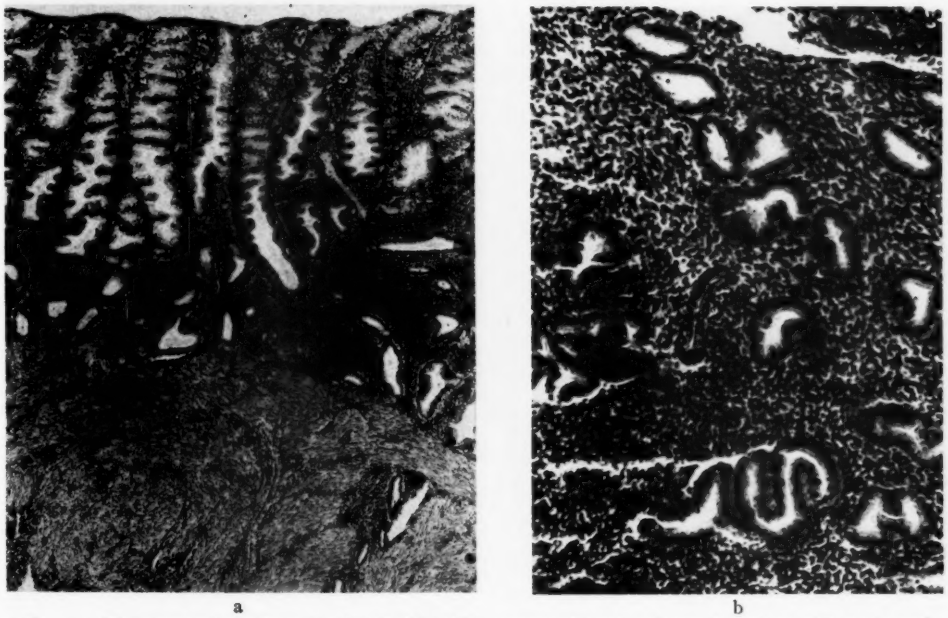
The slides of the endometrium were examined as unknowns. A careful and intensive search was made in each instance for any evidence of decidual reaction. Where decidua was not present the endometria were classified as regenerative (previously termed resting), proliferative, secretory, and menstrual. Moreover, they were dated according to established criteria (12, 5). Thirty-five endometria were proliferative, 45 were secretory, and 7 were menstrual in type. Six were classified as regenerative. Transformation of endometrial stroma to decidua was observed in 22 cases. The findings are summarized in Table II.

TABLE II

Endometrium	Number	Per cent of total
Regenerative or resting	6	5.2
Proliferative	35	30.4
early	20	
mid	12	
late	3	
Secretory	45	39.1
early (17-18 days)	4	
maximal (19-22 days)	12	
exhausted (23-25 days)	21	
premenstrual (27-28 days)	8	
Menstrual	7	6.1
Decidual	22	19.1
Total	115	99.9

Decidual changes associated with ectopic gestation have been noted in only 19.1 per cent of the uterine linings examined in this study. Fourteen of the 22 cases revealed decidua vera which differed in no way from that associated with an intrauterine pregnancy. In the remaining 8 cases involutional changes were present; 3 of these were decidual casts with varying degrees of necrosis.

The proliferative and secretory endometria were histologically similar to those associated with normal ovarian cycles. Twenty of the proliferative endometria were in the early phase. Twelve were considered at the mid-interval period, and 3 were late, i.e. just prior to ovulation. Of the secretory endometria, 4 showed early basal vacuolization and scattered mitoses reflecting recent ovulation following rapid proliferation. Twelve were identified at the height of secretory activity while 21 were in the late secretory phase and



a b

Fig. 1. a, Menstrual endometrium associated with tubal pregnancy. There is characteristic glandular exhaustion, round cell and polymorphonuclear infiltration and predecidual dissolution. ×35. b, Same endometrium. ×130.

exhibited glandular exhaustion. In this latter group, 6 were somewhat atypical because either the glands or the stroma were out of phase. The remainder of the secretory endometria had aggregates of polymorphonuclear and round cell infiltrations with dissolution of sheets of predecidua, indicating the imminent onset of bleeding.

Of the 175 cases reviewed in this study, the ectopic pregnancies in 165 were tubal, 6 were cornual, and there was 1 each of tubo-ovarian, abdominal, and intraligamentary. With the tubo-ovarian pregnancy was an associated proliferative endometrium; with the intraligamentary gestation, an atypical secretory endometrium. Three of the tubal pregnancies coexisted with normal intrauterine pregnancies. Two of these continued uneventfully to term while the third aborted shortly after removal of the affected tube.

DISCUSSION

Frequently, the existence of an ectopic gestation is suspected for the first time when rupture with its associated intraperitoneal hemorrhage and shock has occurred. On the other hand, sometimes this dramatic end result with its striking clinical picture may be the first and only overt manifestation of the disease. From the standpoint of diagnostic alertness, it is unfortunate that the symptom of sudden unilateral lower abdominal pain, accompanied by clinical shock, has been classically taught to be the characteristic picture of ectopic pregnancy. It actually represents a late stage of the disease. In the early phases of ectopic pregnancy, namely, before rupture, the history and findings on pelvic examination are often not conclusive, hormonal tests for pregnancy may be equivocal, and other laboratory aids are of little definitive help. During this phase of the disease various diagnostic procedures have been advocated. These include peritoneoscopy, cul-de-sac aspiration, and anterior and posterior colpotomy. Certain of these techniques, particularly peritoneoscopy, require considerable experience and technical skill on the part of the operator.

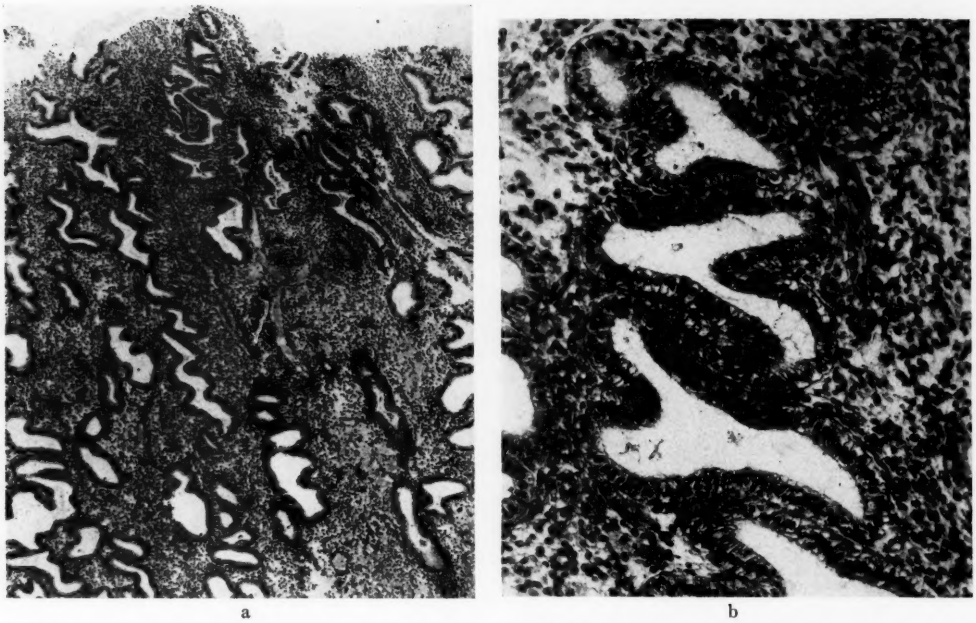


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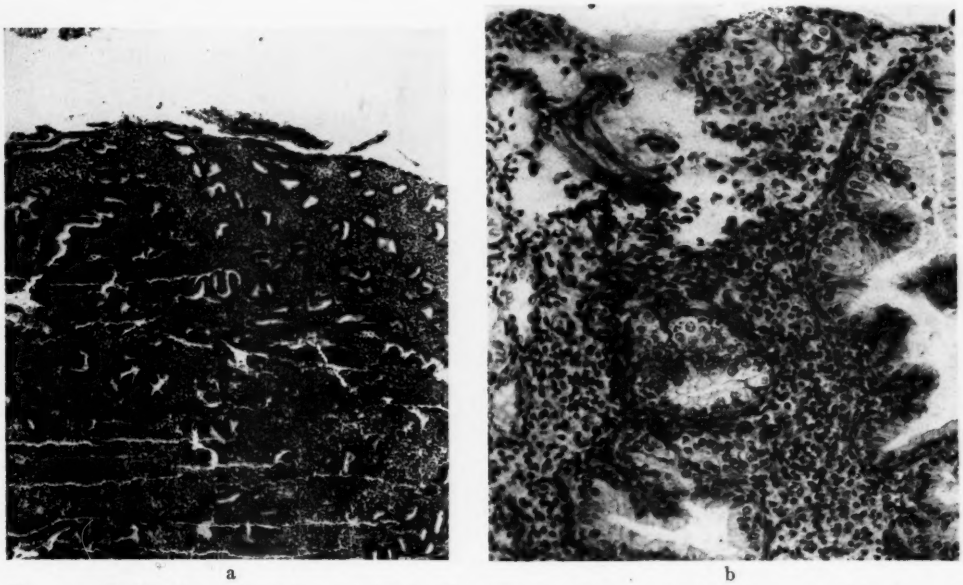
Fig. 2. a, Secretory endometrium associated with tubal pregnancy. The glands are moderately tortuous with basal vacuolization and extensive stromal edema. ×35. b, Higher magnification of section from same endometrium. ×130. The prominent stromal edema and basal glandular vacuoles are easily seen.

Moreover, the information obtained by these methods may be inconclusive or misleading. Irrespective of the value of these techniques, vaginal examination under anesthesia followed by curettage has been considered useful and often necessary in establishing a definite diagnosis.

On the basis of the present and earlier series, the endometria associated with ectopic gestation exhibit the cyclic changes of the menstrual cycle rather than decidual transformation in a high percentage of cases. Gradual decidual transformation of the endometrium follows fertilization regardless of the location of the ultimate implantation site. The hormonal activity of the corpus luteum of pregnancy combined with that of the developing syncytial trophoblast maintains the decidua and inhibits the menstrual mechanism. Both trophoblastic and corpus luteum regression are involved in endometrial involution, and the uterine bleeding phenomenon is a manifestation of hormone withdrawal. In extrauterine pregnancy, the growing conceptus develops a deficit with respect to the adequacy of the circulation at the ectopic placental site resulting in rapid trophoblastic degeneration. This may produce a compromise in the estrogen-progesterone production which has supported the decidual growth. Involution and shedding of the uterine decidua follow either as small fragments or an entire cast. This tissue catabolism may produce a humoral constituent comparable to the menstrual toxin, which the Smiths have found in menstrual discharge (15, 16). This menstrual toxin, a result of the so-called alarm reaction, has a strong pituitary stimulating effect. Variations of endometrial patterns associated with a compromised ectopic pregnancy may reflect an ovarian response to increased pituitary stimulation, the result perhaps of the release of an endotoxin at the damaged decidual placental site. Histologically, the proliferative, secretory, and menstrual endometria in this study were similar to those of the normal ovarian cycle. From



a b

Fig. 3. a, Proliferative endometrium associated with tubal pregnancy. The glands are moderately tortuous. Mitotic activity in glandular elements and in stroma is indicative of growth. ×35. b, Same endometrium. ×130.

an endocrinologic aspect, this suggests that the effect of the hormones of the corpus luteum of pregnancy and syncytial trophoblast had been lost and that a resumption of normal nongestational pituitary ovarian-endometrial function had occurred.

Decidua without chorionic villi is suggestive evidence of extrauterine pregnancy although it does not exclude normal intrauterine pregnancy, abortion, or excessive progestational effect related to an active persistent corpus luteum or granulosa cell tumor. Frank has reported a case in which a decidual cast was passed which on microscopic examination failed to reveal any fetal components. The following day, however, an ovum was spontaneously extruded. Moreover, TeLinde and Henriksen have indicated that decidua-like changes of the endometrium are associated with a type of granulosa cell tumor as well as corpora lutea cysts.

The bleeding of associated proliferative endometria suggests dysfunctional flow with estrogen levels which inadequately support growth stimulation. If the estrogen level decreases or teeters below a critical level, the endometrium undergoes regression and bleeding occurs. Secretory endometria are ordinarily infrequently encountered in dysfunctional flow. However, in this series, this type of endometrium was more frequently encountered. The clinical nature of the bleeding from such endometria is suggestive estrogen teetering with focal breakdown of endometrium and spotting over a prolonged interval. Progesterone withdrawal flow, in contrast, is abrupt in onset, more profuse in amount, and usually involves shedding of the entire endometrium. This bleeding subsides within a few days. At this time, it must be stated that the hormonal sequence which adequately accounts for bleeding from secretory endometria is not known.

Three representative cases of ectopic pregnancy associated with menstrual, secretory, and proliferative endometrium are herewith presented. These illustrate the difficulties of diagnosis, the inconstancy of the symptomatology, the variability of the endometrial pattern, and the inability of the endometrium to contribute to the diagnosis of unruptured ectopic pregnancy.

CASE HISTORIES

Mrs. E. R. M., aged 40 years, No. 33,078, was admitted to the Free Hospital for Women on April 20, 1947 with a chief complaint of pelvic pain of several months' duration. Her past history was irrelevant. She had had abnormally prolonged menstrual flow accompanied by incapacitating cramps in the lower abdomen for several months. Her last menstrual period had begun on March 26 (26 days after the previous flow) and lasted 8 days. Physical examination gave no clue to the diagnosis. On exploration, the uterus was 8 by 5 by 3 centimeters in size. One centimeter proximal to the fimbrial end of the left fallopian tube was a hole through the serosal surface, measuring 6 millimeters in diameter. This was filled with old blood clot which was adherent to the adjacent ovary. A total hysterectomy with left salpingo-oophorectomy was performed. Pathologic examination revealed a pregnancy of the left fallopian tube, chronic salpingitis, and a menstrual endometrium (Fig. 1 a and b).

Mrs. I. Q., aged 37 years, No. 35,114, was admitted to the Free Hospital for Women on October 27, 1947 with a chief complaint of soreness in the lower abdomen which interfered with her work. Her past history suggested an attack of pelvic inflammatory disease 4 months prior to entrance. The last menstrual period was reported to have begun on October 13, 1947, fourteen days before hospital admission. Physical examination revealed dark blood flowing from the cervical os, a normal sized uterus and tender irregular induration across the pelvis. At laparotomy, the pelvis was found to be filled with fibrous adhesions between the tubes, uterus, and rectum. A mass of old blood clot, approximately 19 centimeters in diameter, was protruding from the right tube. The left tube was closed with its adjacent ovary densely adherent to the broad ligament. Pathologic examination revealed a 17 day secretory endometrium (Fig. 2 a and b), a right tubal pregnancy, and bilateral follicular salpingitis.

Mrs. D. C. G., aged 32 years, R.H. No. 5006, was readmitted to the private pavilion of the Boston Lying-in Hospital on December 28, 1947 with a chief complaint of excessively prolonged uterine bleeding. Her last normal menstrual period was October 6 to 8, 1947, approximately 3 months prior to admission. The past history was negative. On November 2, which was 2 days before her next anticipated period, she had had some vaginal staining which continued until November 25 and was followed by a day of flowing consisting of a moderate amount of dark blood. The latter was consistent with menstrual bleeding. There were no other complaints. Hospital admission was elected for the first time on December 5, 1947. She was still flowing. Under anesthesia, the uterus was normal in size. There was a "lemon-sized" mass in the right vault which was thought to be the ovary. A curettage was performed which yielded an abundant amount of normal appearing curettings. Microscopic examination revealed a mid to late proliferative endometrium with minimal hyperplasia. It was presumptively considered that she had a follicular ovarian cyst and she was discharged under close observation. Subsequent questioning revealed an occasional element of discomfort in the right lower quadrant of the abdomen. The mass appeared to be enlarging on pelvic examination. She was, therefore, readmitted for exploration which was performed on December 29, 1947. The right tube was bulbous and measured 7 by 3 by 3 centimeters. A mass resembling organized blood clot, 3 centimeters in diameter at its distal portion, was adherent to the posterior leaf of the broad ligament. A right salpingectomy was performed. Pathological examination revealed a right tubal pregnancy, and mid to late proliferative endometrium. The glands were moderately tortuous and there was some mitotic activity within the stroma (Fig. 3 a and b).

A review of these cases reveals that none exhibited the symptomatology, namely, amenorrhea, unilateral lower quadrant abdominal pain, or manifestations of shock and intraperitoneal hemorrhages which have more commonly been attributed to ectopic pregnancy. The menstrual histories, while not necessarily normal, do not suggest amenorrhea. Pain is quite variable and not prominent. In the unruptured state, symptoms of shock are absent. These histories and their endometria emphasize several important facts. Firstly, it is impossible to establish a diagnosis of extrauterine pregnancy from endometrial examination. Secondly, ectopic pregnancy in its early or unruptured phases presents a vague, nonspecific history, and it is erroneous to consider the dramatic clinical manifestations of rupture as being invariably characteristic of the disease. Thirdly, ectopic pregnancy cannot be excluded from any differential diagnosis in a woman of the childbearing period by reason of laboratory or clinical criteria. Finally, the diagnosis of extrauterine pregnancy in the unruptured state requires a careful clinical appraisal of history and pelvic findings.

CONCLUSIONS

1. Examination of 115 endometrial linings associated with proved ectopic pregnancies revealed 39.1 per cent to be secretory, 30.4 per cent to be proliferative, and 6.1 per cent to be menstrual in type.

2. Histologically, these endometria were indistinguishable from comparable phases of the normal menstrual cycle.

3. Decidua without chorionic villi was present in only 19.1 per cent of the cases studied. Failure to find decidua in endometrial curettings, therefore, does not rule out an existing ectopic pregnancy.

4. Three representative cases of ectopic pregnancy associated with a menstrual, proliferative, and secretory endometria are presented. These emphasize the difficulties of diagnosis, the variability of the endometrial pattern, and its nondecidual nature.

5. An explanation, based on accepted physiologic information, is offered as to the sequence of events producing a given associated endometrium.

6. There are as yet no reliable diagnostic laboratory procedures which establish or exclude ectopic pregnancy in a differential diagnosis. Ectopic pregnancy must be considered in any female in the childbearing period who presents a pelvic diagnostic problem.

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VESICOSIGMOIDAL FISTULAS COMPLICATING DIVERTICULITIS

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THE intent of this survey is to present the findings of an investigation of the clinical course, diagnostic methods, and surgical treatment of diverticulitis of the sigmoid complicated by the formation of vesicosigmoidal fistulas. It seems imperative that the nature of a disease should be determined before any treatment is undertaken to correct the situation. For this reason, this study includes only those cases in which the diagnosis of diverticulitis associated with vesicosigmoidal fistulas was made by a pathologist after careful examination of the segment of the sigmoid removed at operation. Too frequently, one encounters reports of surgical or medical management of vesicosigmoidal fistulas when the causative factor has not been definitely determined. In 1909, Parham and Hume emphasized that the first fact to be established in a logical approach to the problem of vesicosigmoidal fistulas is the exact nature of the underlying disease.

In a study of 25 cases of vesicointestinal fistulas, Ormond, Best, and Klinger reported that the causative factors were trauma in 3 cases, neoplasm in 14 cases, and inflammation in 8 cases. In 6 of the 8 cases in which the fistulas were of inflammatory origin, they were secondary to diverticulitis and all were situated in the sigmoid.

Sutton, in a report on vesicosigmoidal fistulas 28 years earlier, found that the commonest cause was abscess in the region of the uterine adnexa. The next commonest cause was diverticulitis, and the least common cause was carcinoma. The apparent decrease in the incidence of abscess in the region of the uterine adnexa is undoubtedly due to the use of the sulfonamide and the antibiotic drugs.

Gouverneur, Soupault, and Latifi, in an investigation of 324 cases of diverticulitis, found 38 cases of vesicosigmoidal fistulas, an incidence of 11.1 per cent. In the majority of the 324 cases, the presence of diverticulitis was not proved histologically. In some of the cases of vesicosigmoidal fistula, colostomy was the only surgical procedure that had been performed.

From the Division of Surgery, Mayo Clinic and Mayo Foundation.

MATERIAL

In a period of 10 years, namely, from 1939 to 1948 inclusive, 202 cases of proved diverticulitis of the large intestine were observed at the Mayo Clinic. Vesicosigmoidal fistulas were found in 46, or 22.8 per cent, of the 202 cases. In the entire series of 202 cases, the sigmoid was the only portion of the large intestine which was found to communicate with the urinary bladder. This situation is easily explained when one recalls that diverticulitis is more prone to develop in the sigmoid than it is in other portions of the large intestine and that a portion of the sigmoid is in intimate contact with the bladder.

In the 46 cases in which a vesicosigmoidal fistula was present, 39 of the patients were men and 7 were women. The ratio of males to females, therefore, was approximately 5 to 1. It is highly probable that the uterus serves as a barrier to perforation between the sigmoid and the urinary bladder. A hysterectomy had not been performed on any of the 7 women who had a vesicosigmoidal fistula. The youngest patient was 29 years of age, and the age of the oldest patient was 76 years. The average age of the 46 patients was 52 years.

SYMPTOMS

In most of the cases, the chief symptom was referable to the urinary tract. Five of the 46 patients eventually had symptoms caused by intestinal obstruction. Twenty-one patients complained of dysuria or urinary urgency or frequency. The longest duration of these symptoms was 8 years, the shortest duration was 3 days, and the average duration was 18.5 months. Because of the nature of these symp-

toms, most of the patients had been treated for infection of the urinary tract for several months. The symptoms referable to the large intestine were minimal when compared with the intense distress caused by involvement of the bladder.

Pneumaturia was present in 40 cases. The longest duration of this symptom was 13 years, the shortest duration was 2 days, and the average duration was 17.3 months. Pain situated in the suprapubic, perineal, or genital region was present in 14 cases. The longest duration of the pain was 5 years, the shortest duration was 9 days, and the average duration was 16.8 months.

Twenty-one of the patients had passed feces from the urethra. The longest interval that had elapsed since the first observation of feces in the urine was 8 years, the shortest interval was 2 weeks and the average interval was 14 months. Hematuria was present in 10 cases. The longest duration of this symptom was 8 months and the shortest duration was 4 days.

When diverticulitis accompanied by pain and fever adds dysuria or urinary urgency or frequency to the signs and symptoms the indications are bladder involvement. Pneumaturia frequently appeared several weeks later and it is probable that at this stage the fistulous communication between sigmoid and urinary bladder had become well established. Not infrequently, patients stated that they had felt as if "something had broken" and then had noticed a rather explosive passage of blood, urine, pus, and feces through the urethra. Many patients had noticed a very brief period of relief from dysuria and fever after the fistula developed.

Approximately 2 weeks after pneumaturia appeared, pain frequently occurred in the perineal, genital, or suprapubic region. About 3 months after the onset of this pain, the patients usually noticed feces in the urinary stream for the first time. It is logical that gas should appear in the urine before solid particles. The pain which characteristically appeared during the period between the onset of pneumaturia and the appearance of feces in the urine was probably due to the inflammatory process and the engorgement of the fistulous tract with solid material. Approximately 1 year after the appearance of feces in the urine, gross hematuria was noticed in some cases. Hematuria probably was caused by the cystitis and the trauma resulting from the passage of solid material through the fistulous tract.

TABLE I.—ABNORMAL PROCTOSCOPIC FINDINGS IN 18 CASES OF VESICOVAGINAL FISTULA COMPLICATING DIVERTICULITIS

Abnormality	Cases*
Extrarectal mass	6
Diverticula	6
Sacculated sigmoid	4
Fixation of bowel	4
Changes suggestive of fistula	3
Diverticulitis	1
Partial obstruction of bowel	1
Marked angulation of bowel	1

*More than 1 abnormality was observed in 7 of the 18 cases.

Several patients noticed particles of barium in the urine after a barium enema had been administered, and in some cases pneumaturia followed inflation of the sigmoid in the course of proctoscopic examination.

Only 1 patient, a 74 year old man, gave a history of having passed urine from the rectum when the bladder had been full. A history of surgical intervention for removal of a foreign body obstructing the urethra was obtained in only 1 case. In this case, the patient was a man, aged 36 years. Two months before he came to the clinic, a urethrotomy had been performed for removal of a cherry pit. A small fistula persisted in the penis after the operation.

PROCTOSCOPIC FINDINGS

Before surgical treatment was instituted at the clinic, proctoscopic examination was performed in 38 of the 46 cases. In 20, or 52.6

TABLE II.—ROENTGENOGRAPHIC DIAGNOSIS IN 45 CASES

Diagnosis	Cases
Diverticulosis or diverticulitis of sigmoid	31
Diverticulosis or diverticulitis of sigmoid and vesical fistula	8
Obstructive lesion of indeterminate nature	5
Chronic ulcerative colitis and vesical fistula	1

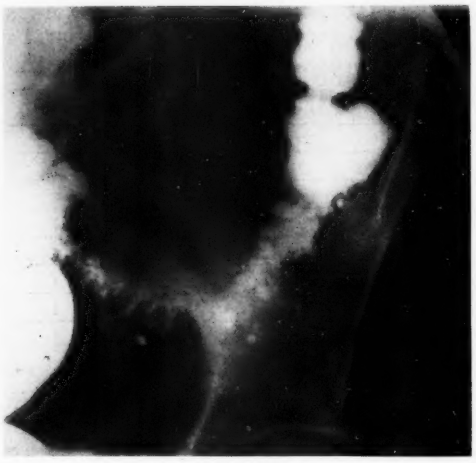

Fig. 1.—Diverticulitis of sigmoid with moderate constriction of intestine.

per cent, of the 38 cases, proctoscopy did not disclose any abnormality. The abnormalities disclosed by this examination in the remaining 18 cases are listed in Table I. It is interesting to note that changes suggestive of a fistula were observed in only 3, or 7.9 per cent, of the 38 cases.

ROENTGENOGRAPHIC FINDINGS

In 45 cases, roentgenologic examination was performed with the aid of a barium enema. Table II shows the diagnosis that was made by the roentgenologist in these cases. A diagnosis of diverticulosis or diverticulitis was made in 39, or 86.7 per cent, of the 45 cases. This examination disclosed a vesicosigmoidal fistula in 8 cases and a fistula of the bladder in another case. It is evident, therefore, that roentgenographic examination disclosed a fistula of the bladder in 9, or 20 per cent, of the 45 cases. Figures 1, 2, and 3 show the roentgenographic findings in a case of diverticulitis in which a vesicosigmoidal fistula developed.

CYSTOSCOPIC FINDINGS

Cystoscopy was performed in 33 cases. In 28, or 84.8 per cent, of the 33 cases, the cystoscopic findings suggested the presence of a fistulous opening in the bladder. Cystoscopy was performed in 13 of the 14 cases of vesicointestinal fistula reported by Barnes and Hill. The cystoscopic examination disclosed characteristic pathologic changes in all of the 13 cases, but the fistulous opening actually could be seen in only 2 cases. One of us (Mayo) and Miller reported that visualization of the fistulous opening was possible in 13 of 30 cases of vesicosigmoidal fistula in which cystoscopy was performed.

To facilitate the detection of a fistulous communication between the intestine and bladder, various organic dyes have been administered orally or rectally, or have been instilled into the bladder. The results produced by the use of these dyes may be misleading.

SURGICAL TREATMENT

In all of the 46 cases in this series, some type of resection of the sigmoid was performed, and the presence of a vesicosigmoidal fistula was verified by examination of the surgical specimen by a pathologist.

Since resection was not performed as an emergency procedure, adequate time was available for preoperative preparation by the medical service in most of the cases. This preparation consisted of the administration of an intestinal antiseptic such as succinylsulfathiazole, the administration of laxatives and enemas, and the use of a low residue diet. In an attempt to correct the loss of protein, fluids, and electrolytes, solutions were administered intravenously and transfusions of blood were given. Recently, antibiotic agents have been used in the preparation of patients for operations on the colon.

In the majority of cases, a colostomy was performed either as a preliminary procedure or as a concomitant procedure with resection. In 5 of the cases, the symptoms persisted and became more severe after the preliminary colostomy was performed. The usefulness of a preliminary colostomy is dependent upon its diverting the fecal stream proximal to the vesicosigmoidal fistula and permitting the inflammatory process to subside before a more definitive surgical measure is undertaken. Colostomy alone has little to offer with respect to permanent relief of symptoms. When this operation is performed, it is imperative that the 2 loops of bowel be well separated to

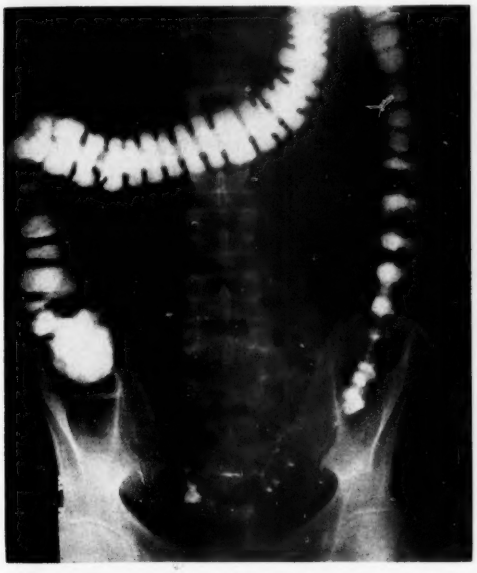

Fig. 2. Diverticulitis of the sigmoid with considerable obstruction of the intestine. This roentgenogram was made about 1 week later than that which is shown in Figure 1.

Fig. 3. Roentgenogram made 3 years later than that shown in Figure 2. The intestinal lumen is more adequate but sinus tracts lead from involved segment; one undoubtedly communicates with the bladder.

avoid spillage of feces from the proximal into the distal loop.

In 2 cases in this series, the vesicosigmoidal fistula was divided and the openings in the sigmoid and bladder were closed. In one of these cases the operation was performed at the clinic, and in the other case the operation was performed elsewhere. In both cases, there was a return of the previous symptoms. In 1888, Cripps pointed out that such an operation was impractical because the sutures were placed in infected tissue. Actually, some type of resection is necessary before any permanent relief from symptoms can be obtained.

An anterior resection with end-to-end anastomosis and a concomitant colostomy was performed in 19 cases. Next in frequency was an extraperitoneal obstructive type of resection without colostomy, which was performed in 15 cases. An extraperitoneal resection with a catheter colostomy in the proximal barrel was performed in 10 cases. In 2 cases, a one stage anterior resection and end-to-end anastomosis was performed without colostomy.

When an exteriorization type of resection was performed, the opening in the bladder was repaired when the segment of sigmoid was exteriorized. When an anterior resection was performed, the opening in the bladder was repaired simultaneously. There were 8 cases in which a suprapubic cystostomy was performed at the time of resection of the sigmoid. In all except 1 of these cases, the patients were men.

ASSOCIATED DISEASE

In addition to the vesicosigmoidal fistula a sigmoidocutaneous fistula was present in 8 cases, an ileosigmoidal fistula was present in 1 case, and carcinoma of the sigmoid was present in 3 cases.

MORTALITY

In 3, or 6.5 per cent, of the 46 cases, the patients died in the hospital. In 2 of these cases, death was due to peritonitis; in the remaining case, the cause of death was not determined.

SUMMARY

This paper is based on 46 cases in which vesicosigmoidal fistula complicated diver-

ticulitis of the large intestine. Thirty-nine of the patients were men and 7 were women. The ratio of males to females, therefore, was approximately 5 to 1. The most logical explanation for this difference is the intervention of the uterus between the sigmoid and bladder. The ages of the patients ranged from 29 to 76 years, the average age being 52 years. The average duration of symptoms was 16.8 months. Proctoscopic, cystoscopic, and roentgenographic examinations are indicated in cases in which the presence of a vesicosigmoidal fistula is suspected.

Surgical treatment is indicated in cases in which a vesicosigmoidal fistula complicates diverticulitis of the large intestine. The operation that was employed most frequently consisted of some type of extraperitoneal resection of the sigmoid and closure of the opening in the bladder. Next in order of frequency was resection of the sigmoid with end-to-end anastomosis and a preliminary or concomitant colostomy. The operation that was employed least frequently consisted of resection and end-to-end anastomosis without colostomy.

In 3, or 6.5 per cent, of the 46 cases, the patients died in the hospital. The preoperative and postoperative use of antibiotics has added much to the safety of resection of the large intestine.

It is the opinion of one of us (Mayo) that primary resection of the sigmoid with or without colostomy and closure of the vesical opening will be employed with increasing frequency in the treatment of vesicosigmoidal fistula complicating diverticulitis.

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THE USE OF B COMPLEX AND VITAMIN C FOR THE PREVENTION AND ELIMINATION OF NAUSEA AND VOMITING FROM DIETHYLSTILBESTROL

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DIETHYLSTILBESTROL has demonstrated its usefulness in a large variety of conditions in obstetrics and gynecology. In obstetrical practice it has proved to be our most useful drug, when administered in adequate dosage, for the prevention of threatened and habitual abortion, premature labor, and some other late accidents of pregnancy. In gynecological practice, it has proved to be a valuable medication for the treatment of various ovarian deficiencies such as dysfunctional uterine bleeding, oligomenorrhea, most menometrorrhagias and many cases of dysmenorrhea, senile vaginitis, and endometriosis. It is of real value as an adjunct in the treatment of vaginal infections. One of the disadvantages of synthetic (as well as natural) ovarian therapy is the occurrence of nausea and vomiting in a certain percentage of cases in the nonpregnant woman.

The incidence of side reactions following stilbestrol was given as 10 per cent by Novak and 6.12 per cent by Hepp in a discussion of a paper by Abarbanel and associates. Various writers have shown that when side reactions from stilbestrol are compared upon a potency basis or even upon a weight basis with those from estradiol or estrone or estrone sulfate the toxic effects are similar in the experimental animal. Stilbestrol, estradiol, estrone sulfate given in 5 or more milligram doses will all cause approximately the same side reactions (Castrodale, Bierbaum, Helwig and Macbryde, Page, Russell, Schwabe, Matthews and Emery). Abarbanel and associates have shown that the incidence of side reactions increases with increased dosage. These side reactions seldom occur in pregnant women.

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For approximately 10 years the author has been investigating methods to prevent or eliminate nausea and vomiting caused by the administration of stilbestrol. The methods found to be of value are enumerated in Table I.

TABLE I.—METHODS FOUND TO BE VALUABLE IN CONTROLLING STILBESTROL SIDE REACTIONS

1. The sipping of sour milk or other mildly acid drinks.
2. The use of pentobarbital sodium capsules or rectal suppositories.
3. The taking of stilbestrol at about 9 p.m.
4. The administration of purified triple crystallized stilbestrol.
5. The administration of micronized stilbestrol.
6. Persistency of treatment. Patients should continue to take tablets because tolerance develops in 4 to 7 days in 95 per cent of cases.
7. The use of vitamin B_6 (pyridoxine) (Patton, 15).
8. The use of antihistaminics (Finch, 7).
9. Very gradual increase of the dose of micronized stilbestrol.
10. The administration of soluble B complex intravenously.
11. The administration of vitamin B complex plus vitamin C by mouth.
12. The use of micronized stilbestrol combined with B complex vitamins including folic acid plus vitamin C in the form of a tablet.
13. The administration of testosterone propionate intramuscularly and orally.
14. The administration of progesterone intramuscularly and orally.
15. The administration of progesterone plus testosterone propionate simultaneously intramuscularly or orally.
16. The use of vitamin C.

COMMENT

By sipping sour milk or other mildly acid drinks, mild secondary nausea may be eliminated in some patients.

By giving 3 grains of pentobarbital sodium by mouth with the first and second 9 p.m. stilbestrol doses, most patients do not experience the first day nausea and vomiting. If subsequent stilbestrol reactions occur, ½ grain suppositories of pentobarbital sodium are given per rectum every half hour until nausea and vomiting are controlled. While this method is

effective, it naturally causes drowsiness and sleepiness.

By making the time of the stilbestrol administration 9 p.m. the patient is usually asleep during the time when the maximum side reactions would occur.

When stilbestrol tablets are manufactured by a process involving triple crystallization, impurities are eliminated and so side reactions are lessened. Furthermore, by administering micronized stilbestrol, a smaller dosage of stilbestrol will be found to be necessary. A micronized stilbestrol crystal is about 0.5 micron in size. (A red blood cell is 7.5 microns.) The minute size of the stilbestrol particles permit their rapid absorption through the gastrointestinal mucosa into the blood stream, so less stilbestrol is required and results are produced quicker.

Persistency of treatment eliminates symptoms in 4 to 5 days because, if stilbestrol is continued, the patient becomes tolerant to the medication in 95 per cent of the cases. This observation has been true not only in our own clinical experience but comparable observations have been made by other writers. For instance, Patton (15) in 1945 gave stilbestrol in 5 milligram doses per diem for functional ovarian disorders to a series of 107 patients. Approximately half had some nausea for the first 2 or 3 days. Nine and three-tenths per cent stopped taking the drug because of extreme nausea. If the patient persisted in taking the medication for 3 or 4 days despite the nausea, the symptom was not noted during the rest of the period of treatment. Very few patients had severe nausea during the entire course.

Patton (16) in 1949, advocated the use of pyridoxine intravenously in all patients complaining of nausea or vomiting after stilbestrol administration, stating that he based his employment of this vitamin upon the success which it had achieved when used by other writers in the treatment of the nausea and vomiting of pregnancy (Silbernagal and Burt, 18, 19). A single dose of 50 to 100 milligrams of pyridoxine was given intravenously and repeated daily if necessary to all patients who complained of severe nausea or of vomiting after starting the 20 day oral course of stilbestrol (5 mgm. daily). This treatment reduced by two-thirds the number of patients unable to take stilbestrol on account of vomiting.

Finch (4, 5, 6, 7) regards the side effects following stilbestrol as due to an allergic reaction identical with the nausea and vomiting of pregnancy. In 1938, he treated such cases by injecting graduated doses of progestin (Finch, 4). In 1942, he adopted the treatment of gradually building up a tolerance to stilbestrol (6), stating that since it is possible to cure the nausea and vomiting of early pregnancy with desensitizing doses of corpus luteum extracts, it was decided to endeavor to "desensitize" patients to the side effects of stilbestrol by administering a course of graduated doses of this drug, hoping that they would eventually become able to tolerate a therapeutic dose. Oral desensitization consisted in giving 0.1 milligram tablets once daily for 5 days, then increasing the daily dose by 0.05 to 0.15 milligram every 5 or 6 days until the therapeutic level required was reached. In every case, the drug was well tolerated after the desensitization process.

Good results have been obtained with the desensitization process. The dosage schedule differs slightly from Finch's. The patient starts with 0.05 milligram of vitaminized micronized stilbestrol daily, increasing the dose 0.05 to 0.1 milligram every 4 days until 6.0 milligrams are being taken. After this dosage level has been reached, the patients can usually tolerate 6.25 milligrams (¼ of a 25 milligram vitaminized micronized stilbestrol tablet), increased by another fourth every 4 days.

In Finch's (7) most recent article, he advocates the use of antihistaminics, reporting a series of 11 cases of nausea and vomiting following stilbestrol, all being benefited by antihistaminics. A few patients complained of drowsiness or dizziness from the antihistaminic drug but within 2 or 3 days they developed a tolerance to it. In this respect, Finch has been more fortunate than some other writers. Schwartz in a series of 217 cases mentions side reactions in 62 per cent of cases in which was used one of the two antihistaminics employed by Finch. In these patients 42.9 per cent developed drowsiness. Some had as

many as four types of reactions simultaneously. In an editorial early in 1950 (3) warning has been given against the use of antihistaminics. The reasons given are that they will result in certain well known side reactions which are manifested by drowsiness, nervousness, and lack of concentration and alertness in those who are susceptible. Finch follows the same procedure in starting his antihistaminics as we use with stilbestrol medication; viz., giving a single tablet at bed time. He then gives additional tablets throughout the day as tolerance is established. The treatment by antihistaminics offers the objection that the side reactions from the antihistaminic may be more severe than the one from stilbestrol so why burden the antiallergic processes of the body with building up two antiallergins when one should suffice and when highly satisfactory alternative treatments are possible?

NEW METHODS OF TREATMENT FOR STILBESTROL REACTIONS

Testosterone propionate (50 to 100 milligrams) given intramuscularly the day of the first 9 p.m. dose of micronized stilbestrol has lessened the nausea and vomiting in 85 per cent of 60 patients. Testosterone propionate having some progesterone-like properties, apparently neutralizes or reacts with some of the stilbestrol leaving a small amount free which aids in desensitizing the patient to the stilbestrol, yet the desired stilbestrol results are obtained even when given simultaneously with testosterone propionate. When only one dose of testosterone propionate is given intramuscularly, the effect lasts for about 7 to 10 days and at the same time stilbestrol is administered nightly and increased every fourth night so a higher and higher blood level of stilbestrol is produced. This stilbestrol blood level increases so gradually that the amount of free stilbestrol is so small that reactions to stilbestrol occur less frequently. If secondary reactions should occur, 50 milligrams of testosterone propionate intramuscularly or by mouth usually will control it.

Patients become tolerant to stilbestrol very much more readily when testosterone propionate is also present in the blood stream 4 to 8 hours prior to the time stilbestrol enters. When testosterone propionate is given 24 hours before the stilbestrol administration, the results are much better still. The larger the amount of testosterone propionate there is in the blood stream, the surer it is that the side reactions from stilbestrol will be lessened or eliminated. In cases in which no emergency stilbestrol is necessary the patient is given testosterone propionate intramuscularly the day before the 9 p.m. dose of stilbestrol.

Testosterone propionate in a dosage of 10 milligrams three times daily and at bed time orally, if given for 7 to 10 days as a supplement to intramuscular testosterone propionate, will aid in preventing nausea and vomiting.

Progesterone in a dosage of 50 to 200 milligrams intramuscularly lessened or eliminated stilbestrol reactions similarly to testosterone propionate in 27 of 30 patients.

Progesterone and testosterone propionate, 50 milligrams of each simultaneously intramuscularly, lessened or eliminated stilbestrol reactions in 27 of 30 consecutive patients.

Vitamin C in 50 milligram daily dosage reduced stilbestrol reactions 25 per cent.

In 80 consecutive patients, the giving of 1 to 5 cubic centimeters of soluble B complex intravenously prevented or eliminated the reactions to stilbestrol in 75 of 80 patients. If given the day of the first 9 p.m. dose, it usually prevents subsequent stilbestrol reactions for 4 to 7 days at which time it may be repeated if necessary. If secondary reactions occur, soluble B complex intravenously will control reactions in from 5 to 30 minutes and will prevent recurrence for 4 to 7 days. B complex can be repeated daily if indicated or at any time that reactions recur, without any untoward effects.

The giving of B complex vitamin tablets by mouth three times daily and at bed time has also greatly aided in inhibiting or lessening stilbestrol reactions.

We have found that the best and most efficient stilbestrol combination consists of micronized triple crystallized stilbestrol combined in one tablet with an ample dosage of B complex vitamins including folic acid plus added vitamin C. The administration of this form of stilbestrol therapy aided greatly in lessening stilbestrol reactions in 40 consecu-

tive nonpregnant patients. Thirty eight experienced no vomiting; most patients experienced mild reactions. Forty nonpregnant patients who served as controls were given plain 6.25 micronized stilbestrol tablets without B complex and 38 had nausea and vomiting.

Recently it has been found that folic acid and possibly other B complex vitamins are essential in estrogen metabolism (9, 10, 11, 12). A possible deficiency of these vitamins in 6 to 10 per cent of the women who manifest side reactions while under stilbestrol medication may explain this condition.

ROUTINE USED IN GIVING VITAMINIZED MICRONIZED STILBESTROL

Fifty to 100 milligrams of testosterone propionate are given intramuscularly and 1 cubic centimeter of solubly B complex is given intravenously on the day before the 9 p.m. dose of stilbestrol (¼ of a 25 mgm. desplex tablet).

If the patient ever experiences stilbestrol side reactions, soluble B complex is repeated and the stilbestrol dose is reduced by ¼ tablet and increased ¼ tablet every seventh instead of every fourth day.

CONCLUSIONS

1. The possible cause of nausea or vomiting following some cases of stilbestrol administration would appear to be due to a deficiency of folic acid and possibly some of the other B complex vitamins which apparently are essential to estrogen metabolism.

2. The use of B complex separately and intravenously aids greatly in reducing stilbestrol reactions. Comparable results are obtained in a great many cases by the use of tablets of micronized stilbestrol combined with B complex including folic acid plus vitamin C.

3. Vitamin C has been shown to aid in reducing stilbestrol reactions and is therefore included in the tablets.

4. Stilbestrol has been found to be inert (nonestrogenic) where an apparent deficiency of folic acid and possibly other B complex vitamins occurs. This condition can be corrected by prescribing micronized stilbestrol tablets containing these vitamins.

5. The routine giving of testosterone propionate intramuscularly and by mouth plus the administration of soluble B complex vitamins intravenously and incorporating B complex and vitamin C with micronized stilbestrol in tablets has made stilbestrol reactions negligible.

6. The technique and dosage of testosterone propionate and soluble B complex for intramuscular and intravenous injection have been described in detail as well as how to deal with recurrences should they take place.

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EDITORIALS

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NOVEMBER, 1950

WAR AND THE DOCTOR

FARSIGHTED Winston Churchill already has said that if you are fighting an octopus it is fatal to begin the struggle by attempting to lop off one tentacle after another but far better to go for his heart. In that connection, it may well be that we are witnessing the beginning of World War III and will not be long content to struggle at the periphery. If world war comes, the medical men of our country must not be caught in the same predicament that our Army found itself in Korea, unprepared.

Any single individual, as the writer, is uninformed as to the detailed steps that are being taken to meet the situation but all of us who have lived through two world wars are deeply concerned to see that the gains made in medical service to the armed forces in the past wars be maintained and that current new problems be actively considered. In this task the civilian medical personnel who were largely responsible for the outstanding record made in the last war should be called upon again for activation of a comprehensive program. The eventual responsibility for the care of the sick and wounded will fall on the civilian doctor.

No one of this generation will soon forget the service of civilian medical men who in the last war placed the procurement and assignment of medical men on a sound basis, the work of the National Research Council, or the outstanding accomplishments of a group of consultants and specialists who perfected the organization of work at the front and at the base which resulted in the best treatment of the wounded with the lowest mortality in our history. Nearly sixty thousand well trained civilian doctors wrote a proud chapter.

None of these feats just happened. They were the result of hard work and careful planning by a skilled and carefully selected group.

If another world war comes, there are problems to meet that will challenge the most enlightened. The effects of atomic energy on the large centers of population supersedes them all. New York State and others have already drawn large scale plans. Every center of oil, steel, manufacturing, and transportation is faced with manifold problems in which the education of the public on the medical aspects of atomic bombing, the care, evacuation, and disposition of injured play important roles. It is obvious that hospital staffs in urban communities should be taking these matters very much to heart. Our student, interne, resident, and nursing bodies are vitally concerned in the best organization possible to meet the situation.

In the last war, a high average was reached in assigning medical men to work for which they were trained. The Surgeon General, however, was placed under the command of the

Commanding General, Army Service Forces, and that is his position today. Loyal Davis has given the matter much thought and I quote from his article[1] which should be read by all medical men. "The complexity of organization which makes it necessary for the Surgeon General or surgeon of a theater to go down the line of command beginning with the commanding general of the service force to the chief of staff or theatre commander and then down to the commanding general of a ground or air force to implement matters which concern the treatment of the wounded invites delay, confusion, and inefficiency." There are many other consequences of this type of organization which should be corrected before another world war is upon us.

In a world war the civilian population will be subjected to risks that may involve large casualties. The doctors who by necessity or decree stay at home to care for the homefront, to carry on medical education and research and to staff our large charity hospitals not only carry a large burden of responsibility but are in the unenvious position of staying at home during an all out war effort. It would clarify the position of essential teachers and investigators if an official list of such men was announced at the beginning of a world war and they were given commissions in the armed forces.

There can be little doubt as to the obvious necessity of being prepared, in a medical sense, for a large scale world war. The civilian doctor will be called upon in a large measure to meet the necessities of the situation. Would it not be wise for our responsible national medical organizations to start at once in a comprehensive program that at least would not leave the medical profession unprepared to take its place in the war effort?

VERNON C. DAVID.

[1]Surg. Gyn. Obst., 1945, 81: 702-704.

THE ADRENAL CORTEX

SURGICAL research has long focussed its attention on those biological properties of the patient which render wound healing possible and favor survival after extensive trauma. "We dress the wound, God heals it" may be paraphrased "we dress the wound, the patient heals it"; the inherent survival-reaction of the patient grows in importance as surgical technique extends its horizons and antibiotics control invasive sepsis. An understanding of these biological properties makes the surgeon's care rational and his therapy effective. Evidence brought forward in recent years places the adrenal cortex and its related neuro-endocrine mechanisms at the focal point of this research.

That a pattern of metabolism followed injury was shown by Cuthbertson; Selye gave it a name—the "alarm reaction"—and a mechanism when he showed that adrenalectomy or hypophysectomy abolished many features of the response. It remained for Thorn to give us a simple test of the adrenal response to stress—the eosinophile test—and the broad outline of the road map is complete. Filling in the details of this new road map, putting in the "stop and go" lights and tracing the highways which avoid trouble will render obsolete many of the congested routes we now follow. We may then steer clear of detours such as wound dehiscence, "unexplained" hypotension and shock, metabolic decompensation with uncontrolled salt loss and prolonged postoperative morbidity.

Our first task is to understand the physiology more clearly. Recent work demonstrating a hypothalamic center for suprapituitary control of the pituitary-adrenal response to stress is of central importance. It appears to localize the intersection of nervous pathways and hormonal mechanisms in the central nervous sys-

tem. The role of epinephrine in initiating adrenocortical activity in response to trauma places this mechanism among those sympatho-adrenal phenomena described by Dr. Cannon as protecting homeostasis in emergencies. The water-retaining and sodium-retaining effect of adrenocortical discharge and the mobilization of cell water and protein which follow injury combine effectively to bolster extracellular water and plasma volume. This may be interpreted teleologically as providing the organism with additional volume in the vascular bed after injury. Alterations in cell permeability, renal tubular function and protein synthesis are the metabolic mechanisms whereby this reorganization is accomplished.

A second task is to outline in greater detail the metabolic effect of this pituitary-adrenal discharge. A negative balance of nitrogen and potassium occurs, with sodium and water retention; the potassium loss outstrips nitrogen loss and returns sooner to positive balance; an increased expanse of body water is available for sodium solution: all these are characteristic of the metabolic response to operation. That large doses of adrenocorticotropic hormone produce similar changes (with differences in the handling of nitrogen) is a fact of importance. Starvation alone produces certain of these responses although sodium is lost, rather than retained; adrenalectomized animals on adequate replacement will also show nitrogen losses in response to local tissue trauma, the adrenalectomy having removed adrenal activation from the equation. Immobilization alone produces a miniature metabolic response in the same direction as operation despite the absence of any clear-cut increase in excretion of 17-ketosteroids or corticoids. These studies all point up the fact that the adrenal is not playing a solo; starvation, tissue destruction and immobilization join the chorus. The total result is the metabolic response to surgery.

The postoperative salt intolerance which has been emphasized so fruitfully by Coller and Moyer appears to be a manifestation of the salt-retaining "desoxycorticosterone-like" effect of adrenocortical discharge. The diuresis of sodium 14 to 16 days after surgery is less well known; it is one of the most constant after-effects of trauma. Indeed the "drying out" of the patient about two weeks after major surgery is a result of this diuresis. It signalizes one of the important milestones in convalescence. The excretion of the urinary end-products of adrenal hormones provides another quantitative measure of adrenal response. Correlation of steroid excretion with types of surgical convalescence may turn out to be more informative than changes in metabolic balance or circulating eosinophiles.

A third task for the future is to understand the effects on the convalescent process of abnormalities in this endocrinology. Addison's disease, myxedema, lesions in the pituitary region and other endocrine disorders may all be expected to abolish the response of the organism to stress. These conditions are rarities; though important they may hardly be considered an everyday problem in surgery. It is much more important to emphasize that borderline endocrine abnormalities, combinations of age, debility, and cachexia, may occasionally produce hyporesponsiveness of the normal stress mechanism. This potentially dangerous situation may be diagnosed by abnormalities in the eosinophile response to epinephrine, ACTH, or adrenal cortical extracts. The use of these three agents serially will permit accurate localization of the site of the adrenal "block." The eosinophile response is a remarkably sensitive one; drops in eosinophile count will be shown in response to the most minor degrees of trauma and in very extensively debilitated people. Potassium loss or sodium retention is less sensitive as an index of trauma-response

and patients who are extremely debilitated may show little electrolyte shift while their eosinophiles drop in a normal fashion. The urinary excretion of hormone end-products as steroids in the urine is an even less sensitive index of adrenal reaction. By these means we may study the patient's endocrine response to injury; replacement treatment with hormone preparations is yet in its infancy.

There is no evidence that the metabolic response to trauma is in any way deleterious to the patient when the rate and magnitude of gain or loss are of normal amount and duration.

There is a tendency, for instance, for patients after extensive surgery to show transient drops in the serum potassium level with an apparent gain in extracellular water. This situation has been called "potassium deficiency." This misnomer should not be applied to those changes which occur after trauma in the normal individual any more than the decreased urine output after trauma should be referred to as "urine deficiency." These are responses of the normal human being to trauma and are correlated with normal convalescence. When the same set of mechanisms operate in the face of pre-existent water and salt depletion (especially where metabolic alkalosis exists) they produce the full blown picture of "hypokaliemic alkalosis" with oliguria, hypotension, alkalosis, low plasma potassium, electrocardiographic changes, muscular weakness and a critically ill patient. The normal response to stress might be called "hypokaliemic alkalosis in miniature"; the normal response to ACTH is identical. There is no rationale nor indeed any justification for pouring large amounts of water, potassium, nitrogen or chloride into the average postoperative patient in order to reverse this natural trend.

The fourth task at hand is to define the relationship of this neuro-endocrine axis to wound healing, the tensile strength of wounds and the microscopic anatomy of the healing process. Here the evidence is conflicting. Secondary incisions made in animals five to seven days after an initial trauma heal with greater tensile strength than the initial wounds. Yet we might reasonably expect that chronic stimulation of the pituitary and adrenal by repeated traumas would inhibit wound healing because of the suppression of fibroplasia which follows the administration of ACTH or Compound E. A normal stress response may be correlated with normal wound healing and set the stage for wounds of increasing strength; chronic stress may inhibit fibroplasia. The collagen diseases have been described as the "healing process greatly overmagnified"; their progress is interrupted, even if only temporarily, by adrenal hormones. There is a relation here to surgery. It is important to elucidate this relationship. Do wound dehiscence, thromboembolism, liver or kidney failure correlate with hypernormal or hyponormal adrenal responsiveness? We know from experience that surgery in Addison's disease or myxedema may be dangerous because of hyporeaction of the adrenal axis. Do other abnormalities of this endocrine system endanger our patients in ways of which we are now blissfully unaware? May alterations in adrenal function influence the immune response of the surgical patient struggling against a septic process? Or the immune response to homologous grafts of skin or viscera?"

Many important questions are raised by these facts discovered in laboratories throughout the nation. There are few solid answers. Here is a challenge to the surgical investigator.

FRANCIS D. MOORE.

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THE BOOK SHELF

THE DEVELOPMENT OF THE MEDICAL MOTION PICTURE

THOMAS E. KEYS and LEONARD A. JULIN, Rochester, Minnesota

WRITING on "The Cinematograph as an Aid to Medical Education and Research," Dr. Rudolph Matas in 1912 in his presidential address before the Southern Surgical and Gynecological Association said (38):

"I have . . . sought . . . to direct your attention . . . in the value and availability of another method of photographic reproduction, which I believe far surpasses all others in inherent interest, educational value, and in its immense though undeveloped possibilities for the scientific and technical training of the men of our craft."

Today even more so than in 1912 Dr. Matas' remarks are seen to have been fully justified. It seems worth while, therefore, to consider the origins and the development of medical motion pictures in order that their present place in medical education might be better evaluated.

THE CAMERA OBSCURA

The principle of the camera obscura was well known in classical times. Euclid used a darkened room to teach the rectangular propagation of light in the observation of sunbeams through small apertures. Moreover, Aristotle showed that the sun's image always was round although the light passed through a square aperture. Alhazen, the Arabian philosopher, who died in 1038, was the first to point out that in the eye the pattern of the retinal image corresponds to that of the object which faces the pupil. Leonardo da Vinci, about 1500, also discussed the camera-like structure of the eye and illustrated the phenomenon of vision with diagrams. The camera obscura fitted with a lens was described by Giovanni Battista della Porta (*c.*1538–1617) in the first edition of his book, *Magia Naturalis*.[1]

Although the camera obscura was soon applied to the science of cartography, it would appear that its first recorded use in the field of medicine was achieved by the English anatomist and surgeon, William Cheselden, who published his osteographic atlas in 1733. On the title page of this work, there is an illustration showing his use of the camera obscura (Fig. 1).

THE MAGIC LANTERN

The magic lantern is an optical instrument having lenses for training upon a screen magnified pictures from slides placed in the focus of the outer lens. It is generally considered an outgrowth of the camera obscura and is usually thought of as the invention of Athanasius Kircher who described it in 1646. There is reason to believe it to be of an earlier origin. J. Voskuil has recently reviewed the subject. In studying Kircher's original work, Voskuil found that the magic lantern is traceable back to the old art of mirror writing, which can be traced back to Pythagoras (*c.*500 B.C.). Figure 2 shows Kircher's magic lantern. In 1668, Robert Hook described a cam-

Mr. Keys is librarian and Mr. Julin is director of photography, Mayo Clinic.

[1]This was the first draft of Giovanni Battista della Porta's *Magia Naturalis* published in twenty books in 1589. An English edition of this work was published in 1669 as follows: "Natural Magick . . . in Twenty Books . . . Wherein Are Set Forth All the Riches and Delights of the Natural Sciences." London: John Wright, 1669. [2p. 1., 409 pp., 3 1. 8°]. Book seventeen of this work is entitled "Of Strange Glasses." In this chapter (pp. 363–365) is found the following: "Before I part from the operations of this glass, I will tell you of some use of it, that is very pleasant and admirable, whence great secrets of nature may appear unto us as, To see all things in the dark, that are outwardly done in the sun, with the colours of them. You must shut all the chamber windows, and it will do well to shut up all holes besides, lest any light breaking in should spoil all. Only make one hole . . . if you put a small centricular crystal glass to the hole, you shall presently see all things clearer. . . ." We are indebted to the Army Medical Library for the loan of this volume.

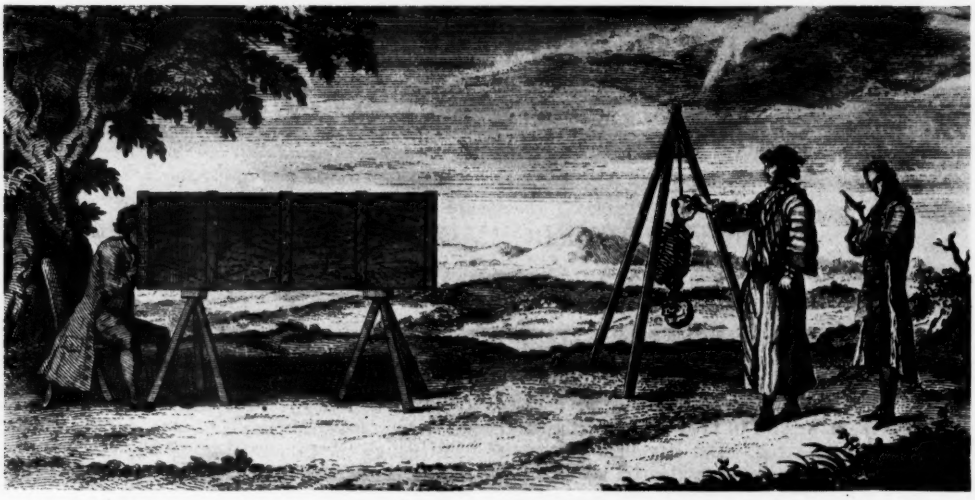

Fig. 1. Camera obscura devised by William Cheselden for the accurate drafting of the bones of the human body. It is traditionally reported that the figures represent Vander Gucht, the artist, John Belchier posing the skeleton, and Samuel Sharp taking notes. (Reproduced from the title page to vol. 1 of William Cheselden, 13.)

era lucida which was used as a magic lantern. Images of illuminated and inverted objects were projected by means of a broad convex lens through an aperture into a room where they were viewed by an audience.

PHOTOGRAPHY

In 1727, Johann Heinrich Schulze (1687–1744), imprinted shadow pictures on a salt precipitate of silver in a bottle. It was well known prior to his time that daylight had a blackening effect upon silver salts. Carl Wilhelm Scheele (1742–1786) discovered in 1777 that blue light was more effective than red light in reducing silver salts, and in 1800, ultraviolet light was discovered through its photographic action by Johann Wilhelm Ritter. Thomas Wedgwood (1771–1805) also attempted to perpetuate images. The results of experiments which he made with Sir Humphrey Davy were published in 1802. Wedgwood was able to produce shadow negatives or silhouettes.

Some of the earliest photographs were those of Joseph Nicéphore Niépce (1765–1833). Niépce was able to obtain a negative only, since he knew of no way of reversing the negative in order to get a positive print. His first photographs were produced in 1827. On December 14, 1829, Niépce formed a partnership with Louis Jacques Mondé Daguerre (1787–1851) who had been working on a new photographic process. Upon Niépce's death in 1833, Daguerre entered into partnership with Niépce's son, Isidore. In the Daguerre photographic process, a silver-coated plate was polished, fumed with iodine, exposed, developed and fixed in hot brine. Exposure took about 15 minutes. Daguerre and Isidore Niépce let this formula be made public in return for a pension by the French government (1839).

William Henry Fox Talbot, working independently, made a positive image directly from a negative (66). A series of experiments led in 1835 to the production of impressions in the camera by means of silver chloride. He employed paper sensitized with salt and silver nitrate to produce paper negatives. He used these negatives to produce positive prints. On January 3, 1839, he described his photographic process before members of the Royal Institution and a few days later before members of the Royal Society (8).

Sir John Herschel (27), the astronomer (1793–1871), worked with hyposulfurous acid and its compounds in 1819. In 1839 he (28) showed how a photographic picture could be made permanent by dissolving the unaffected silver salts in a bath of "hyposulphite of ammonia" (hypo). In 1839 a French civil servant, Hippolyte Bayard, invented a method by which a positive print could be made directly by sensitizing paper with silver salts and exposing it in a camera.

Another improvement came about after the discovery of collodion in 1846 by Menard in Paris and independently by Parkers Maynard in Boston

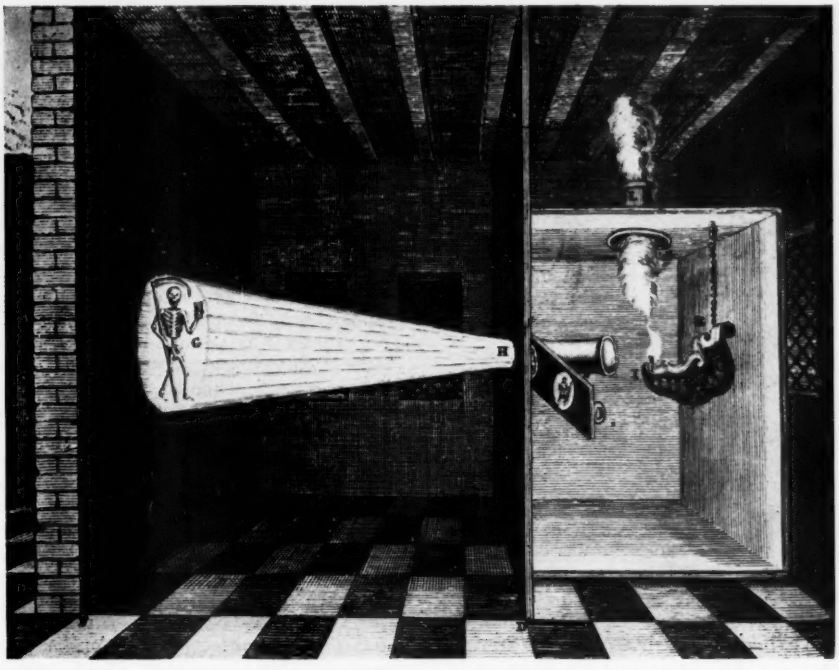

Fig. 2. The magic lantern of Athanasius Kircher from his *Physiologica Kircheriana Experimentalis* (Amsterdam, 1680) p. 126. (Reproduced by permission of the Army Medical Library.)

in 1848 (11). In 1851, Frederick Scott Archer, an artist of English descent, announced the wet collodion process.

A big improvement was the "dry plate" or gelatin emulsion process. This is usually attributed to R. L. Maddox, an English physician, who wrote about it in 1871, but in 1868 William H. Harrison had already outlined a process and Carey Lea of Philadelphia had suggested a dry process a year previously.

MOTION PICTURES

The illusion of movement upon which the cinema depends must have been known since early times. According to Lubschez, Ptolemy in 130 A.D. actually demonstrated the phenomenon of persistence of vision by means of revolving spots. The shadow shows of the ancient Chinese (6) and the magic lantern, earlier referred to, bear a relationship to the modern motion picture. Another aspect was the development of optical toys. One of these was the "dazzling top" of the Abbé Nollet (6). Another important concept occurred in 1825 when Sir John Herschel (68) showed Sir Charles Babbage how it was possible to see both sides of a coin at once by spinning a shilling at a certain speed. Babbage mentioned this phenomenon to a Dr. Finton. A few days later, Finton presented Babbage with a disk of cardboard suspended between two cords of silk. On one side of the disk appeared a likeness of a bird (Fig. 3); on the other side, that of an empty cage. If held in front of one's eyes and rotated rapidly, the revolving disk produced the effect of a bird in the cage. In the 1830's Dr. Plateau of Ghent and Dr. Stampfer of Vienna invented almost simultaneously and independently similar disks showing the illusion of motion in pictures and depending for their effects upon the persistence of vision (64). Dr. Stampfer called his instrument the "stroboscope" and Dr. Plateau named his the "phenakistoscope." In the phenakistoscope (Fig. 4), the disks revolved on a common shaft. The front disk had several phases of a moving object drawn upon it. The drawings were placed near the outer edge. The back disk was larger and had radial slots in it. When in operation (with the aid of a mirror), the phenakistoscope established the principle of the intermittent shutter. Many similar devices were later invented. One of the most im-

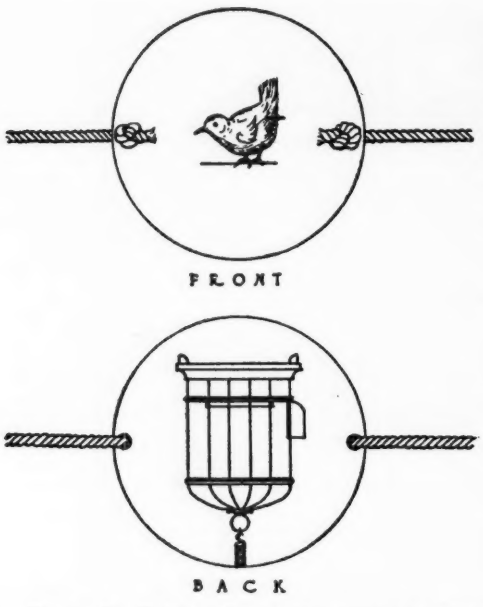

Fig. 3. Dr. Finton's thaumatrope, invented in 1825. (Reproduced by permission, from B. J. Lubschez, 35, p. 12.)

portant of these was the kinematoscope (Fig. 5). This was patented by Dr. Coleman Sellers (1827–1907) on February 5, 1861 (45).

While the photographic process was in the stages of being perfected, Eadweard Muybridge (1830–1904), was given an unusual assignment. It came about as a result of a controversy. The problem which undoubtedly had been posed frequently before was to settle for once and all whether or not a horse while trotting or even at the height of his speed ever had all 4 of his feet off the ground simultaneously.[1] To find out if this actually happened, Muybridge (40) began his investigations on the race track at Sacramento, California, in May, 1872. The problem was to obtain a sufficiently well developed and contrasted image on a wet collodion plate, after an exposure of such a brief duration that a horse's foot, moving with a high velocity, could be photographed.

To find the answer, Muybridge made several negatives of a celebrated horse, "Occident." The photographic results were sufficiently sharp to give a recognizable silhouette portrait of the driver, and some of them exhibited the horse with all of his feet clearly lifted, at the same time, above the ground! It then occurred to Muybridge that a series of photographic images made in rapid succession at properly regulated intervals of time or of distance would definitely be of use in studying animal movements.

Muybridge discussed his plans with Governor Leland Stanford, who made it possible for Muybridge to continue his research at Palo Alto. John D. Isaacs, according to Quigley (46), devised a battery of cameras to take consecutive photographs at very short intervals for the experiments. The process was named "chronophotography." Figure 6 shows several equidistant consecutive views of a horse while trotting. These were first published, along with several hundred other illustrations, in 1882, in the book *The Horse in Motion* (65). To show synthetically the reproduction of animal movements, Muybridge devised the "zoöpraxiscope." Using stereoscopic pictures he placed the appropriate halves in 2 of Plateau's zoetropes. The zoetropes were revolved at the same rate of speed, and by the aid of mirrors the stereographs were made visible and the result was a satisfactory reproduction of an apparently real miniature horse trotting and of another horse galloping. One evening in 1879, Governor Stanford invited a few friends to witness by projection with the oxyhydrogen light the results of Muybridge's endeavors (39). Muybridge was by no means the first person to project photographic images to demonstrate the persistence of vision. As mentioned by Cameron, Beale of Greenwich, England, photographed movement analytically and projected it in 1854. Many other similar investigations followed that of Beale.

Owing to the efforts of Dr. William Pepper, Muybridge (43) was able to continue his photographic efforts at the University of Pennsylvania. He had as his chief assistants Dr. W. D. Marks, professor of dynamical engineering at that university, and Thomas Eakins, the American artist. Their combined efforts resulted in a profound study of animal locomotion. His pictures of motion proved later to be of scientific value to physicians studying movements of patients afflicted with locomotor ataxia, lateral sclerosis, spasms, convulsions, and paralysis. Muybridge later continued his studies on human beings, and in 1901 published *The Human Figure in Motion* (39).

Using Muybridge's technique, Dr. Edward Reichert, according to Nitzche, took pictures of the movements of a dog's heart.

[1] In 1872, Governor Leland Stanford of California bet $25,000.00 that the legs of a horse running at full gallop were off the ground simultaneously. He hired Muybridge to get photographic proof. See Quigley (45, pp. 118–119).

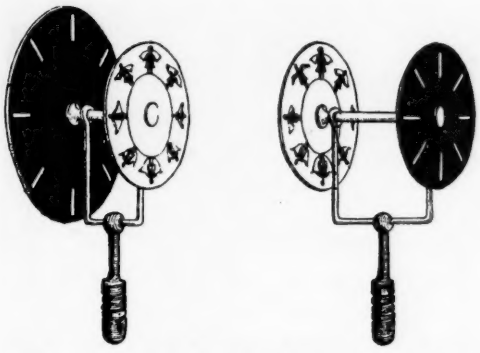

Fig. 4. Dr. Plateau's phenakistoscope (about 1833). Left, early form used with mirror; b, later form, direct view. (Reproduced by permission from B. J. Lubschez, 35, p. 15.)

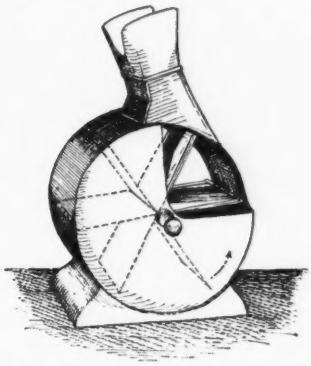

Fig. 5. Dr. Coleman Sellers' kinematoscope (1861). (Reproduced by permission from B. J. Lubschez, 35, p. 26.)

This was apparently the first time (1887) that a motion picture was used in medical research. In the light of present day endeavors, Reichert's technique was most interesting.

In the course of anesthesia, a portion of a dog's ribs over the heart was removed and a battery of cameras was placed before the dog in such a way that a series of pictures showing the successive phases of the contraction and dilation of the heart were obtained. Positive prints were made from the negatives. These were placed in Muybridge's zoöpraxiscope, and the action of the dog's heart was shown on the screen.

Muybridge's projected images were primitive motion pictures; however, the pictures were not taken at equal intervals of time because the speed of the subjects varied during the course. Furthermore, the pictures were not taken from the same viewpoint but as if the spectator ran along the row of cameras. Because of this, Muybridge's pictures were not entirely satisfactory.

The problem of taking pictures at equal intervals of time was solved by the physiologist, Étienne Jules Marey (1830–1904). In 1882, by placing a revolving shutter into a camera, Marey was able to take a picture every hundredth of a second.

Pierre Jules César Janssen (1824–1907), invented the astronomical revolver in 1873 (37). Meanwhile, Marey had been working on the idea of a photographic gun based on Janssen's astronomical revolver. He perfected it late in 1882. Marey's photographic gun (Fig. 7) contained a long focus objective in its barrel. In the breach of the gun was a revolving circular plate. Marey first used his gun to study the flight of birds. According to Quigley (47), Marey's photographic gun was the first practical motion picture camera.

A serious handicap in the projection of motion pictures was the glass plate. This limited the number of scenes that could be run off in succession. The idea of an endless band of pictures instead of a disk with pictures on the outer edge probably was thought of early. The German photographer, Ottomar Anschuetz, as mentioned by Stenger (62), arranged his negatives in sequence in his "tachyscope" invented in 1887. Anschuetz demonstrated his results publicly in 1891. In 1889, Marey had presented motion pictures of street scenes obtained by the use of film pulled and held in position by a system of cams and gripping plates (11). Motion pictures were made practicable by Thomas Alva Edison (1847–1931). Edison used a strip of flexible collodion film to carry the photographic emulsion. Then he invented a machine, the "kinetograph," which could be used for the taking of motion pictures by photography. It was then necessary to develop a machine for viewing the moving pictures. He gave to the machine the name, "kinetoscope." The kinetograph, according to Quigley (48), was the first motion picture camera that could photograph a few seconds of action at a time. The kinetoscope, according to Lubschez, was first shown in public at the Brooklyn Institute in May, 1893.

Meanwhile, George Eastman (1854–1932) desired to make photography popular. He realized that the glass plate was too cumbersome. After trying gelatin in 1884, he began to manufacture a roll form of photosensitive paper to be used with a camera. In 1889, Eastman applied for a patent on

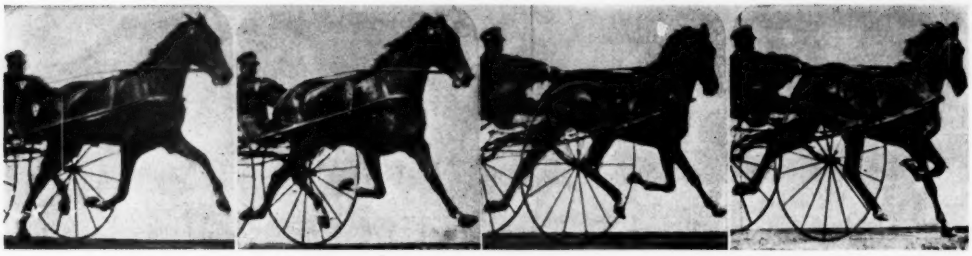

Fig. 6. Muybridge's trotting horse experiments in photography. (Reproduced by permission from Eadweard Muybridge, 40.)

the manufacture of transparent flexible photographic films (49). Two years previously, the Reverend Hannibal Goodwin, working independently, obtained a patent on "photographic pellicle," which is described as transparent, sensitive and like celluloid (51). Soon after Goodwin's endeavors, Eastman began the manufacture and marketing of a celluloid photographic film. A legal battle between Goodwin and Eastman took place. Goodwin died and Mrs. Goodwin won the suit. Eastman's patent was finally issued in 1898. Meanwhile, he had been supplying Edison with all of his film. Edison made the projection intervals of the pictures equal by perforating the film and guiding it through the machine with the aid of sprocket wheels. In 1895, August and Louis Lumiére, of Lyons, improved on Edison's apparatus by inventing a claw movement to move the film intermittently (50). The Lumiéres developed a satisfactory apparatus, the "cinématographe," which was patented in 1895. In 1895, then, the foundations of the modern cinema had been laid and many inventors in America and Europe added their discoveries to further improve the motion picture.

MEDICAL MOTION PICTURES

As mentioned previously, the first known motion picture of a medical subject was Reichert's study of the heart beat of a dog in 1887. Greenhill suggested that P. Schuster made the first medical motion picture in 1897. It demonstrated pathologic complex body movements. Doyen, of Paris, allowed himself to be filmed while operating, in 1898 (24). Oskar Messter also produced motion pictures (Fig. 8) of operations at the Surgical Clinic of the University of Berlin in 1898 (63).

Interestingly enough, Doyen is also said to have filmed an operation performed by Professor Ernst von Bergmann. This was for an amputation of the leg below the knee, for which the date, 1903, has been assigned (24). Doyen left behind him, when he died in 1916, an impressive series of motion picture films; among them was one showing the surgical separation of Siamese twins, which was made in Berlin.

The first medical motion pictures of patients in the United States were made at Boston by Dr. Walter Greenbough Chase. In 1905, Chase used the "biograph," an apparatus made by the American Mutoscope Company, for demonstrating pathologic motion. With this device, he made motion pictures of 21 separate epileptic seizures. The idea of reproducing various pathologic gaits had been attempted earlier, according to Chase, by Dr. Alex McLane Hamilton with the aid of the Lumiére camera. Chase also mentioned that some work along this line was initiated at the Saltpetrière Hospital in Paris. Apparently, Baron Henri de Rothschild, who at one time was a medical student, also used the biograph to show surgical methods at the Rothschild Hospital. Dr. Chalot's method of treating Pott's disease was screened with the aid of the biograph.

Motion pictures were not used extensively in medical teaching until after the end of the first world war, chiefly because the universities lacked the necessary equipment. Kaufmann, pointed out that in Germany, even during World War I, a center for scientific motion pictures was established by August Bier and Curt Adams. The first informal medical film library was established by the German firm U F A in 1919. By 1922, according to Greenhill, U F A listed 150 medical films in its catalog. In 1922, also, an institute dealing only with medical cinematography was founded at the University of Berlin. In Great Britain and the United States, the production of medical films for teaching was relegated to individual medical faculties. During recent years, however, centers have been established, with the support of industry and government subsidy, for the production and dissemination of teaching films. The Ameri-

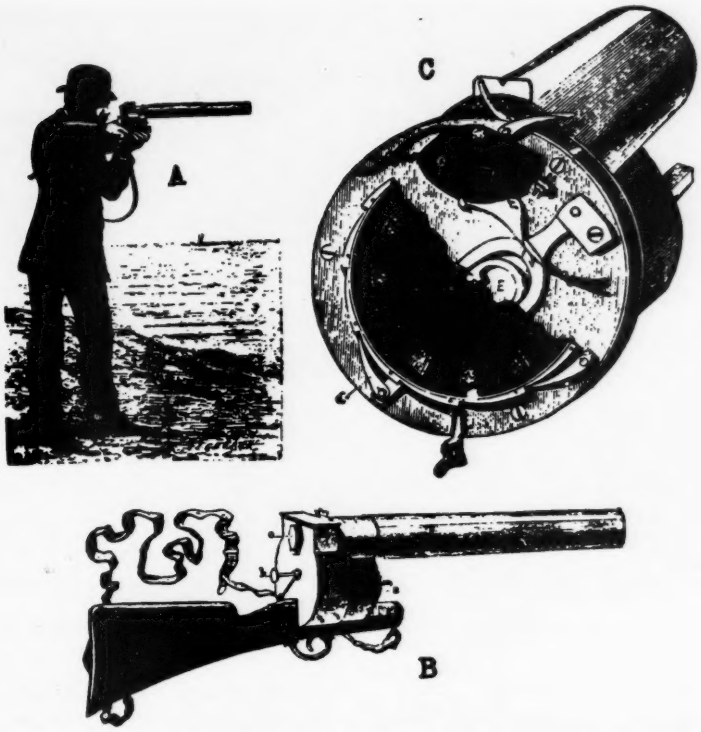

Fig. 7. Marey's photographic gun. A, Marey's design; B, general arrangement of the "gun" showing the extensible "barrel" containing the lens; C, the 12 windowed aperture plate against which the photographic plate was pressed and some of the mechanism for rotating the plate intermittently. (Reproduced from J. R. Cameron, 11, p. 37.)

can College of Surgeons for several years has issued catalogs of approved films. Recently, the American Medical Association (16) has adapted an extensive program for medical films. It does not plan to produce films, but rather to act as a clearing house on matters of information concerning them. One of its most useful endeavors has been the publishing of critical reviews of films in the *Journal of the American Medical Association.*

Kroenig and Sellheim, as mentioned by Greenhill, made the first motion pictures showing labor and gynecologic operations. Albert Doederlein (1860–1941), of Munich, made a "trick" motion picture concerning labor, and Sebastian Recarem y Giral of Madrid made a film showing the development of the fetus. In the field of neurology and psychiatry, Karl Bonhoeffer, of Berlin, produced a motion picture entitled, "Expression in typical Emotional States of the Mentally Disturbed."

Vittonio Putti of Bologna, and René du Bois, Raymond, and others made orthopedic films showing remedial exercises, walking with artificial legs, and the treatment of scars. According to Kaufmann, Maddrick, in England, produced the first anatomic teaching film, a skeleton demonstration. In 1946 H. C. R. Simons, of Zurich, introduced a new method of registering time (dark flash) in making a film of the rapid diagnosis of parasitic blood diseases.

One of the most successful of the early medical films made in the United States was Kanavel's motion picture "Infections of the Hand" (1928). It was produced by the Eastman Kodak Company under the sponsorship of the American College of Surgeons. Tom Jones served as designer and supervisor of the animation.

Fig. 8. First surgical operation to be filmed. Operation was performed in 1898 by Ernst von Bergmann (1836–1907). Oskar Messter was the producer and filmed the operation (31).

CINEROENTGENOGRAPHY

As early as 1897, according to Reynolds (53), Dr. John MacIntyre had the idea of cineroentgenography. He made a short film showing the movement of a frog's leg. It was screened at a meeting of the Glasgow Philosophical Society in 1897. Since the equipment and photographic methods of 1897 demanded long exposures, MacIntyre was not able to use normal motion picture technique. As mentioned by Buckstone, MacIntyre solved the problem by building up animation from a series of separate roentgenograms, which, after being transferred to motion picture film, were projected in the normal way. That same year Roux and Balthazard studied gastric motility in various animals by the use of roentgen rays. They used the photochronographic technique of Marey and made a succession of roentgenograms at regular intervals. They also conducted similar experiments on human beings. N. P. Eykmann, of Holland (*c.* 1901) also thought of using roentgenograms with the cinematograph. In 1908 he reported his apparatus with which he was able to record on zinc plates the movements of the pharynx. He was able to make a series of roentgenograms showing the various phases of swallowing, and he obtained a sort of motion picture record.

In 1909, C. Kaestle, H. Rieder, and J. Rosenthal reported their work on the roentgen-ray cinematography of the internal organs. This they achieved by taking a series of roentgenographic pictures in quick succession. They called their method "bioroentgenography."

There were many technical obstacles to the problem of direct roentgen-ray cinematography. It was difficult to expose the x-ray film rapidly enough to obtain satisfactory roentgenograms. When this obstacle was overcome, no suitable cinematographic apparatus was available for producing a continuous series of pictures because of the size of the film. J. Carvallo (22) of the Marey Institute of Paris, using a film 60 millimeters in width and 57 millimeters in length, was able to illustrate the process of digestion in worms, frogs, mice and chickens. By using a double thickness of sensitized paper and the principle of intermittent motion, he overcame many difficulties. The animals to be tested were fed a certain alimentary paste which was mixed with bismuth nitrate and given with the usual food.

In 1912, Comandan and Best, according to Buckstone, made a kineradiographic film of a canary in a cage. The film showed a canary's skeleton hopping about the cage.

Russell Reynolds (52) produced the first kineradiographic films of much medical value. He established the indirect method in which the roentgenographic image on the fluorescent screen was photographed on 16 millimeter film. He began this work in 1921 and obtained rapid serial roentgenograms of the moving organs of the body and of movements of the joints in health and disease. With the technical assistance of George Little, Dr. Walter C. Alvarez began building an apparatus for roentgen cinematography in 1926. This apparatus made from 1 to 6 roentgenograms per second. In 1933, A. E. Barclay, according to Buckstone, introduced a direct system of kineroentgenography. His method consisted of making a series of roentgenograms on a roll of x-ray film and reducing the copy so that it could be projected as a motion picture.

CINEPHOTOMICROGRAPHY

Besides his many contributions to the development of cinematography, much credit must be given Étienne Jules Marey for his work in the field of cinephotomicrography. In 1894, according to Heard (25a) he adapted the motion picture camera to a study of motions which take place in the field of the microscope.

Pizon, according to Richards, photographed the development of a colony of the tunicate Botryllus. He showed the pictures at the 1904 Zoological Congress at Berne. Ries, as mentioned by Richards, studied the fertilization and division of the sea urchin egg in 1908 by using photochronographic equipment loaned to him by the Institute de Marey.

Jean Comandan in 1909 filmed bacteria, spirochetes, and colloidal particles. Comandan encountered many technical difficulties, especially the vibrations from the machinery of the cinematograph and the lack of proper lighting. The technical difficulties were later obviated to a great extent by the introduction of microscope incubators, powerful filament lamps, and the synchronous motor drive.

Another early worker in this field was Walter Buckstone of the medical department of Kodak Limited, of England. In 1909, he assisted a Mr. Pigg in the preparation of some cinephotomicrographic films of biologic subjects.

The first cinephotomicrographic film showing the growth of tissue cultured in vitro was made by Braus, in 1911, working in Sidentopf's laboratory at the Carl Zeiss factory in Jena (54). The movements of the chromosomes during the development of the sea urchin were clearly shown in the films made by Comandan and Joly in 1913.

Another important worker in this field was Dr. Canti, of St. Bartholomew's Hospital, who started to make his famous cancer film in 1926.

SOUND MOTION PICTURES

The use of recorded sound with motion pictures came as the result of work done by a large number of individual workers. The subject has recently been reviewed by E. I. Sponable.

In 1929, the earliest medical sound film was produced by Sir Thomson-Walker in Great Britain. The subject was internal urethrectomy. The recording was on a 12 inch (30.5 cm.) synchronized disk. The film was made by the Kodak medical department at King's College Hospital and first was shown to members of the Royal Society of Medicine on June 27, 1929 (10).

In 1930, the first of a series of 25 medical talking films which were to be produced by the College of Physicians and Surgeons, Columbia University, was shown in New York city. This film showed Dr. C. R. Murray setting a broken ankle (5). It was accompanied by a commentary by Dr. Murray explaining his technique. About this time, DeLee made the first motion picture sound film of obstetric procedures.

COLOR

Besides sound, color has been of utmost importance in the development of medical motion pictures. In the early days of photography, many attempts were made to produce colored photographs. In 1861, the British physicist, Dr. James Clerk Maxwell demonstrated the projection of colored pictures (41). From 3 photographs of a piece of colored ribbon, 1 red, 1 green and 1 blue, he made 3 lantern slides. By means of 3 projectors, each with a filter of the same color as that used in making the negative, he projected a colored picture of the piece of ribbon.

This process, known as the "additive process," was later used to produce motion pictures in color. In using the additive methods, it was found difficult to obtain sufficient light on the projection screen and to avoid color fringes in pictures of moving subjects. A modification of the additive process, known as the "screen plate process," was used in some systems (autochrome, Agfacolor, Dufaycolor, Finlay color, and so forth). Instead of 3 plates (or films), a single plate (or film) coated with a layer of blue, red and green filters of microscopic size which is in contact with the light-sensitive emulsion is used in the screen plate process. One drawback to the process is that much of the light is absorbed and the white tones are relatively dark. When the pictures are pro-

jected, the images appear broken up by the small color particles, and in motion pictures these particles appear to be "dancing" on the screen.

The subtractive color process was first described by Ducos du Hauron in 1869, in his book *Photographie des Couleurs*. In this process, 3 separation negatives are made through blue, green and red filters. Positives, made from these negatives, are converted to images of dye or pigment the colors of which are complementary to those of the filters by which the corresponding negatives were made. If these color positives are superimposed on film there results a color transparency suitable for projection (14).

The subtractive color processes have a number of advantages over the additive method. Subtractive color films do not require special projection equipment but can be handled in the same way as black-and-white films and they produce a bright image on the screen.

In endeavoring to find a less complicated process, a number of workers have experimented with three-color monopack film. In 1921, Leopold Mannis and Leopold Godowsky, Jr., conceived of a novel color process. They were musicians and began color photography as a hobby. As a result of their collaboration with the Kodak Research Laboratories, they joined the Kodak staff in 1931, and in 1935 the new Kodachrome process was announced.

ENDOSCOPIC MOTION PICTURES

The principal difficulty in making motion pictures of the inside of body cavities is to provide sufficient illumination of the area to be photographed and to be able to visualize the field while directing the camera. In France, in 1913, L. Chevroton, and F. Vlès used specially designed apparatus to make motion pictures of the vocal cords. As mentioned by Stenger (64), Professor Giulo Panconcelli Calzia, of Hamburg, in 1920 reported successful cinematography of the vocal cords after a series of experiments begun 7 years before. In this country, Le Jeune and others devised equipment for motion pictures of the larynx. Special equipment designed and constructed by J. D. Brubaker, an engineer, has been used to make successful color motion pictures through the proctosigmoidoscope, the gastroscope, and the bronchoscope.

RECENT DEVELOPMENTS

With high-speed cameras, many subjects have been filmed to aid in our understanding of physiologic processes. Recently, as mentioned by Nicholas Kaufmann, the employment of "Schlierinkematographie" by Brandmayer and Rikli has made air currents in breathing, speaking, coughing, and singing visible by film. Through their method, the radiation of the body heat into the air surrounding the body has also been made visible.

One of the most valuable features of the motion picture camera is the fact that it apparently can be used to compress or expand the action that it photographs. Motion pictures are recorded and projected at the rate of 16 exposures per second on silent film, or 24 frames per second with sound-on-film. If the pictures are taken at much greater intervals and projected at normal speed, the action appears greatly speeded. This technique, known as "time-lapse," is often used to record growth of living cells as was so well demonstrated in the Canti films. Action that is very rapid or of brief duration can be recorded at a faster camera speed, and when projected at the usual rate the screen image can be studied with ease. This technique is known as "slow-motion photography" and approximately 150 frames per second is the limit for the motion picture cameras of ordinary design.

High-speed motion picture cameras have a range of from 250 to 10,000 frames per second (57).

High-speed cinematography requires a very high intensity of illumination and the accompanying heat may be harmful to living organisms. A water cell can be used to absorb excessive heat rays, as was done by W. Herriott and D. W. Farnsworth when making high-speed motion pictures of the vocal cords at the rate of 4,000 frames per second (26).

A novel method of illumination was devised by Henry M. Lester. He used photoflash lamps fired in rapid sequence to provide intense light with little heat. By this method, he took pictures at the rate of 3,000 frames per second while photographing the action of the wings of a drone-fly.

Recent discoveries permit the making of roentgenograms with very brief exposures (one microsecond to a tenth microsecond). This permits the making of roentgenographic motion pictures of a rapidly moving subject. A special camera has been constructed to make 100 roentgenograms in one second. A film 9½ inches (24.1 cm.) wide is used and the resulting roentgenograms can be copied onto ordinary motion picture film for projection purposes (60).

COMMENT

It is evident that the motion picture was not the invention of one person but the result of a long series of progressive steps in physics and chemis-

try. Since early motion picture film was not very sensitive to light, it was necessary to use sunlight or carbon arc lamps to obtain adequate photographic exposure. The films were not sensitive to red, and therefore red tissues and blood would appear black and void of detail in the pictures. Panchromatic film, which was sensitive to red, became available about 1914. Faster lenses also were produced, and it was possible to make pictures with less illumination.

During the early years there was a lack of standardization, and films of various sizes were used. Gradually, a film 35 millimeters in width became the accepted size. The hand-cranked cameras were bulky and heavy and required the use of a tripod. In 1923, several lightweight cameras for use with 16 millimeter film appeared. These could be used without a tripod and the handcrank was replaced by a spring motor. A darkroom was no longer necessary because the cameras could be loaded with film in daylight. The cost of both cameras and film was much reduced. The 16 millimeter cameras used a reversal film that could be exposed in the camera and subsequently developed into a positive for use in the projection machine, thus eliminating the cost of making a positive from the negative film as was done previously. Whereas the old films were highly inflammable and constituted a serious fire hazard, the new 16 millimeter films were of the safety type and could be used without a fireproof projection booth. The 35 millimeter size remains standard for theatrical use but the 16 millimeter film and equipment is now known as "semiprofessional" and is used for nearly all films of medical subjects.

Additional improvements were made in color sensitivity, resolution and speed of films, and a new era in surgical filming arrived in 1931, when very fast panchromatic films appeared on the market. Incandescent lamps provided ample illumination for use of this film, and a photographic technique was evolved which has persisted with but slight changes.

From the early attempts at motion picture photography when the workers were handicapped by the limitations of film and equipment, we are now approaching the time when the applications are dependent upon the ingenuity of the workers.

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REVIEWS OF NEW BOOKS

THE new edition of Comroe's *Arthritis and Allied Conditions*[1] has been rewritten by Joseph L. Hollander in co-operation with an outstanding group of physicians. This group of specialists write from experience in the various fields of arthritis, including orthopedics, physical medicine, and internal medicine.

The book has been entirely reorganized and brought up to date. There appears to be better organization and presentation of material than in previous editions. The work is monumental and not only includes the present knowledge of rheumatoid arthritis but also includes many apparently unrelated entities. The reason for this approach apparently is to bring to the attention of the reader the various clinical entities which may cause pain and disability of the musculoskeletal system, which may resemble rheumatoid disease superficially.

The book has been divided into 10 parts, each of which is organized in chapters dealing with the more detailed study of the general subject under discussion.

The first part describes rheumatic diseases in general and covers classification of rheumatic diseases, examination of the patient, structure and function of articular tissues, synovial fluid, and x-ray findings.

Part 2 deals specifically with rheumatoid arthritis and includes in detail descriptions of pathology, clinical picture, laboratory findings, and treatment, including orthopedic as well as medical management.

Part 3 is entitled, "Factors Influencing the Onset or Course of the Rheumatic Diseases." The discussion of the many factors influencing the course of the diseases is theoretical in many cases. A discussion of compound E is included.

Degenerative joint disease is discussed in 3 chapters of part 4 dealing with pathology, symptoms and findings, and treatment. Although the chapter on treatment is rather incomplete and sketchy, the coverage of pathology is generally well done.

Related diseases such as rheumatic fever, fibrositis, and spondylitis in its various forms make up part 5. Other related conditions are included and described briefly.

The collagen diseases and miscellaneous conditions of obscure etiology are discussed in parts 6 and 7 and include such diseases as scleroderma, hemophilic arthritis, and tumors of joints and tendons.

The chapter on gout is well done and makes up the major portion of part 8 which covers metabolic disorders.

There are about 100 well written pages on infectious types of arthritis which cover the subject well. The subjects covered range from tuberculous arthritis to tropical disease and are well worth reading.

Part 10, we believe, could well be omitted from a book of this type. Almost 200 pages are devoted to a discussion of unrelated diseases and conditions principally of an orthopedic nature. These include backache, sciatica, the painful shoulder, and others. Much of this material is covered more adequately and logically in works on the specific topics.

The chief value in the book seems to be the condensing of a mass of information concerning the musculoskeletal system into one book. It is primarily a reference book on the rheumatic diseases and as such is valuable because of convenience. The unrelated topics, however, are covered in other texts and do not need to be included in a book of this type.

WILLIAM A. LARMON.

THE first edition of *Psychosomatic Medicine* by Weiss and English published in 1943 has become a standard reference. Much of what was considered new 6 to 7 years ago is now an accepted part of medical thinking, particularly in the case of young practitioners, residents, internes, and students. It was a rare medical officer who saw military service in World War II who did not return to his practice resolved to understand the psychic factor in illness.

Because so many men were already indoctrinated into the so called psychosomatic concept, it became possible in the second edition[2] to add material on orthopedic and physical medicine and the role of social service work, and to extend the chapter on psychological testing. Case illustrations were also elaborated. The book has been rearranged so that now the first one-fourth is given over to "General Aspects" while the remaining three-fourths are devoted to the psychosomatic disturbances as they appear in the various systems of the body. This makes for easy continuity and for ready reference.

In general the material reads smoothly and the lessons are simply stated so that the doctor, not psychiatrically trained, can utilize them easily. Here and there "psychiatric" language creeps in and, to the uninitiated, the content sounds like "double talk." Such semantic confusion unfortunately is a part of much psychiatric exposition, and until the psychiatrist develops a language which is nonesoteric as regards the average physician, there will be passages whose meaning is not entirely evident to all.

[1] ARTHRITIS AND ALLIED CONDITIONS. By the Late Bernard I. Comroe, M.D. Edited by Joseph L. Hollander, M.D., and collaborators. 4th rev. ed. Philadelphia: Lea & Febiger, 1949.

[2] PSYCHOSOMATIC MEDICINE; THE CLINICAL APPLICATION OF PSYCHOPATHOLOGY TO GENERAL MEDICAL PROBLEMS. By Edward Weiss, M.D., and O. Spurgeon English, M.D. 2d ed. Philadelphia and London: W. B. Saunders Co., 1949.

However, these semantic sins are minimal and *Psychosomatic Medicine* remains one of the most useful books of our era. It has something to offer every physician, be he general practitioner or specialist. Even the psychiatrist can use the content and bibliography as a starting point for further investigations. BENJAMIN BOSHES.

IN the preface to Dr. Hegemann's short but very provocative monograph *Die individuelle Reaktionsweise bei chirurgischen Infektionsprozessen*,[1] he points out that the discovery of the bacterial etiology of various types of infectious processes led to extensive studies regarding the virulence of different strains and the method of their invasion. This tended to overemphasize the role of the invading organism. It is true that immunologists have studied the development of specific immunity during the course of infection and the response to artificial vaccination with specific bacteria, but very little is known of the inherent powers within the body which resist the primary invasion of the micro-organisms, particularly those which produce surgical infections.

The author points out that operative wounds are invariably contaminated by many different organisms coming from the air, from the noses and throats of the operating team, and from the skin of the patient. Yet the great majority of these wounds heal without infection, when the usual precautions are taken which comprise sterile technique as practiced in most hospitals. He also points out that wounds resulting from street accidents, war wounds, and burns are contaminated by many different types of organisms and yet only a relatively small proportion of them become infected. It is therefore obvious that there must be forces within the body which tend to make the individual either resistant or susceptible to infection. These factors are so numerous that it is difficult to analyze them and to determine in any given case what the major factor of resistance really is. It is only within recent years that attention has been directed to these factors and they offer a broad field for research. It is certain that individuals differ from one another in their ability to resist infections, both medical and surgical. There are so many factors involved that they form permutations and combinations which readily explain individual differences. The author considers the major factors to be constitution, heredity, age, hormones, nervous and mental controls, nutrition and metabolism, allergy, trauma, and tissue predilection, and he deals with each factor in its turn in separate chapters of his monograph.

One of the factors which render mankind either resistant or susceptible to infection, is what is called the patient's "constitutional type." This is linked up with the factor of heredity. Both of these are completely out of our control. The age of the patient seems to play a role. The prevalence of certain types of infection in certain age groups has been noted frequently. Some of the factors concerned with growth and the degenerative processes of old age may be directly linked up with susceptibility or resistance to infection. Age may also modify the hormonal factors which of themselves may play a role. They vary not only in quantity in different individuals but in the same individual at different periods of age. The mind and the central nervous system may favor or inhibit infection indirectly, particularly those infections which occur in regions such as the alimentary tract, where the functions of secretion and motility may influence the invasive properties of the normally contaminating organisms. The factors of nutrition and metabolism offer a particularly promising field for research, because these may be brought under direct control.

The author's chapter on mixed infections, secondary infections, and recurrent illness would seem to concern the invading organisms to a greater extent than the body defenses, because the synergism and the antagonism of bacteria considerably modify the extent and degree of invasion. Likewise the chapter on the allergic elements of infection concern the development of sensitivity to specific types of infection, although this sensitivity may be of a general nature and subject to nonspecific therapy.

The factor of trauma is well known and self-evident, but further research offers promising results, particularly with regard to war surgery.

It has been known for a long time that certain bacteria find a favorable environment for their growth and localization in certain tissues, while in other tissues and organs conditions are unfavorable. Further studies along this line are clearly indicated.

The monograph as a whole is of very great interest and should stimulate many aspiring young men to enter this field of research. Although the study of bacteriology and the discovery of the chemotherapeutic agents, particularly the antibiotics, have solved many of the problems connected with surgical infections, so that these may often now be controlled without resort to surgery, there is still opportunity for interesting and profitable research in the field of surgical infections and this monograph points the way. FRANK LAMONT MELENEY.

IN his small volume *Physiology in Diseases of the Heart and Lungs*[2] Doctor Altschule has presented in a concise and, for the most part, clear manner experimental physiological observations which explain wholly or in part clinical and laboratory findings as they occur in diseases of the heart and lungs.

This book is primarily a review of data included in scientific papers and is not intended to be a textbook of physiology. Observations made many years ago, as well as the most recent writings, are presented; consequently, the bibliography is massive and constitutes approximately half of the book. In this re-

[1]DIE INDIVIDUELLE REAKTIONSWEISE BEI CHIRURGISCHEN INFEKTIONSPROZESSEN. By Dr. Gerd Hegemann. Berlin, Goettingen, Heidelberg: Springer. 1949.

[2]PHYSIOLOGY IN DISEASES OF THE HEART AND LUNGS. By M. D. Altschule, M.D. Cambridge, Mass.: Harvard University Press, 1949.

spect, it will serve as a valuable reference guide for those now engaged in or contemplating cardiopulmonary research.

In most instances, Doctor Altschule presents conflicting data and then indicates which, in his opinion, is the most accurate observation. He does not hesitate to point out, however, that certain observations or techniques were faulty and, "like the squid, beclouds the issue."

While this book was written because of interest manifested by advanced medical students, its greatest appeal will or should be to the practicing physician who desires to approach his cardiorespiratory problems with a more scientific outlook. The book should be destined to great popularity and should stimulate the writing of similar treatises on other phases of abnormal physiology. JOHN A. MART.

THE high esteem in which the author (lately deceased) of *A Practice of Orthopedic Surgery*[1] is held by all orthopedic surgeons makes a reviewer of his popular work wish to praise it most highly. The statement in the preface, that advances in orthopedic surgery have necessitated the book's revision will apply to any treatment of the subject before the last decade. It is disappointing, therefore, to find that in this third edition the alterations and revisions have not been more complete. So much of the old material has been retained and so little of the newer understanding of skeletal diseases and of techniques has been added that the book cannot be said to represent a modern presentation of the principles of orthopedic surgery. Particularly with reference to infections of the skeleton, there was need for a complete rewriting of the discussion of osteomyelitis and its treatment. Few will agree with the author that chronic osteomyelitis is little influenced by penicillin. Probably revision was made too early for inclusion of data on streptomycin treatment of tuberculous infections. There are numerous instances of neglect to describe improved methods of treatment. Slipped femoral epiphysis, for example, is not discussed as well as it deserves to be and its early treatment by internal fixation is not mentioned. Among many omissions of important diseases which the orthopedist may treat are: osteoid osteoma, nonossifying fibroma, eosinophilic granuloma, infantile cortical hyperostosis, fibrous dysplasia, and gout.

The book is well indexed and its illustrations are for the most part satisfactory. CLY H. HATCHER.

IN the increase from 3 to 4 volumes plus an index volume, *Modern Surgical Technic*[2] by Thorek begins to approach the voluminous tomes on operative surgery by earlier authors. However, in comparison, many obsolete and unnecessary surgical procedures which were of historical interest only have been omitted. Some system which covers all branches of surgery should be included in the home library of every surgeon, and this work would serve admirably. With the assistance of 12 coauthors, the entire field of surgery is well covered.

Volume 1 is concerned with general operative considerations, principles of plastic surgery, and surgery of the head and neck. The author should be congratulated upon the excellent discussion of general operative considerations, including preoperative preparation, evaluation of the patient, fluid and electrolyte balances, use of blood and antibiotics, selection of anesthetics, problems pertaining to sterilization in the operating room, and the care of the patient and complications postoperatively. These pages may well be read by students and experienced surgeons.

Volume 2 contains excellent dissertations on neurosurgery, vascular, thoracic, and orthopedic surgery. Surgery of the nervous system is covered quite completely and will be of value to the neurosurgeon and the general surgeon who handles neurosurgical cases. Descriptions and illustrations of nerve exposures are fine. The chapter on surgery of arteries is particularly commendable, setting forth the basic principles, techniques, and good illustrations. The chapter on veins is very good. The portion devoted to thoracic surgery is quite comprehensive. It includes practical discussions and fine illustrations of the transthoracic and transthoracoabdominal approaches for gastric and low esophageal lesions as well as recent advances in surgery of the heart and large vessels. In the chapter on orthopedic surgery, the passage concerning the orthopedic service in hospitals is superfluous. Orthopedic surgery has long been accepted as a specialty. The advantages of the plaster of paris cast are emphasized and the pertinent statement that all the new mechanical devices cannot replace it is laudable. The descriptions of operative procedures on the whole are good. The section on fractures is quite clear and concise.

Volume 3 dwells upon surgery of the breast and abdomen, and in it the author is dealing with subjects in which he is particularly interested. The various incisions used in abdominal surgery are well delineated. The author speaks from his own early experience and personal disappointments in bringing out the inadequacy of the small abdominal incision. He does make the statement that it is a well known fact that surgical instruments, sponges, and the like often are left in the body following surgery, particularly in abdominal surgery. This is not altogether true, and in any future edition, the misstatement should be avoided by substituting the word "occasionally" for "often." The stomach and duodenum are well covered with good illustrations of the most important operative procedures, including gastrostomy, vagotomy, and the abdominothoracic approach for total gastrectomy. The small intestine is discussed very practically, but in the illustration

[1] A PRACTICE OF ORTHOPEDIC SURGERY. By T. P. McMurray, C.B.E., M.B., M.Ch., F.R.C.S. (Edin.). 3rd ed. Baltimore: The Williams & Wilkins Co., 1949.

[2] MODERN SURGICAL TECHNIC. By Max Thorek, M.D., LL.D., Sc.D., F.I.C.S., F.B.C.S., D.C.M. With a foreword by Fred W. Rankin, B.A., M.A., M.D., LL.D., Sc.D., F.A.C.S. 2d ed. Vols. 1, 2, 3, 4, and index. Philadelphia, London, Montreal: J.B. Lippincott Co., 1949.

depicting the arterial supply of the large intestine taken from Kirschner's *Operative Surgery*, one is surprised to note that the middle colic artery is either forgotten or mislabelled. This is basic, and the error should not be perpetuated in textbooks dealing with the technique of colon surgery. The principles of gastrointestinal suturing are well recounted. All accepted techniques for colon resection are included in the discussion, both open and closed methods. However, in the discourse on sphincter preserving operations for carcinoma of the rectum, the pull-through procedure is described but the principles of resection and suture are not mentioned. The section on biliary tract surgery is praiseworthy. Pertinent facts on liver function and newer developments in liver and biliary tract surgery are brought out, including complications of ascites and portal hypertension. The author's technique in electrosurgical obliteration of the gall bladder is described at length but he apologizes for his enthusiasm about this procedure. Nevertheless, surgeons must admit its value in selected cases and all surgeons should be cognizant of its applicability. Too little attention is given to details of surgery of the anus and lower rectum. The chapters on the pancreas and spleen are excellent, containing detailed descriptions of accepted techniques. These may be read to advantage by students and experienced surgeons.

Volume 4 deals with hernias, gynecologic operations, and surgery of the genitourinary tract. The résumé of the history of hernia and its treatment is well written. Recent contributions, such as tantalum wire and gauze, are included. The basic principles of gynecologic surgery are presented very practically, and this portion is excellent for the library of the general surgeon or the gynecologist. Both conservative and radical procedures are discussed. The description of anatomy is good in the section on genitourinary surgery. Plastic procedures are well depicted and the factual presentation of the technique of retropubic prostatectomy will be helpful to those interested in developing this technique.

This work is a distinct improvement upon the older, more voluminous systems of operative surgery, and it is hoped that future editions will tend toward contraction rather than expansion into additional volumes.

R. Russell Best.

BOOKS RECEIVED

Books received are acknowledged in this department, and such acknowledgment must be regarded as a sufficient return for the courtesy of the sender. Selections will be made for review in the interests of our readers and as space permits.

Post-Graduate Lectures on Orthopedic Diagnosis and Indication. By Arthur Steindler, M.D., F.A.C.S. Springfield, Ill.: Charles C Thomas, 1950.

Immortal Magyar; Semmelweis, Conqueror of Childbed Fever. By Frank G. Slaughter, M.D. New York: Henry Schuman, Inc., 1950.

The Hinge Graft or Ginglymus Implant. By Arnold K. Henry, M.B., Dubl.; M.Ch.(Hon.), Cairo; F.R.C.S.I. Baltimore: The Williams & Wilkins Co., 1950.

Pneumoconiosis; Beryllium Bauxite Fumes. Edited by Arthur J. Vorwald, M.D., with the collaboration of Manfred Bowditch, A.B., Thomas M. Durkan, M.E., and Theodore C. Waters, L.L.B. 6th Saranac Symposium. New York: Paul B. Hoeber, Inc., Medical Book Department of Harper & Brothers, 1950.

Biological Standardization. By J. H. Burn, D. F. Finney, and L. G. Goodwin. 2d ed. London, New York, Toronto: Geoffrey Cumberlege Oxford University Press, 1950.

Facial Paralysis being a Treatise on a Clinical Classification of Paralysis of the Facial Nerve. By J. Parkes Findlay, M.B., Ch.M. Published by the author and distributed by Angus and Robertson Ltd., Sydney.

Cancer of the Colon and Rectum; its Diagnosis and Treatment. 2d ed. By Fred W. Rankin, B.A., M.A., M.D., LL.D., Sc.D., F.A.C.S., and A. Stephens Graham, M.D., M.S., F.A.C.S. Springfield, Ill.: Charles C Thomas, 1950.

Diseases of the Foot. By Emil D. W. Hauser, M.S., M.D. 2d ed. Philadelphia & London: W. B. Saunders Co., 1950.

New and Nonofficial Remedies; Containing Descriptions of the Articles which Stand Accepted by the Council on Pharmacy and Chemistry of the American Medical Association on January 1, 1950. Issued under the direction and supervision of The Council of Pharmacy and Chemistry. Philadelphia, London, Montreal: J. B. Lippincott Co., 1950.

Annual Reprint of the Reports of the Council on Pharmacy and Chemistry of the American Medical Association. With the Comments That Have Appeared in *Journal of the American Medical Association*, 1949. Philadelphia, London, Montreal: J. B. Lippincott Co., 1949.

Transactions of the Southern Surgical Association; Sixty-First Annual Meeting Held at Homestead Hotel, Hot Springs, Va., December 6, 7, 8, 1949. Philadelphia, Montreal, London: J. B. Lippincott Co., 1950.

Eyes and Industry; Formerly Industrial Ophthalmology. By Hedwig S. Kuhn, M.D. 2d ed. St. Louis: The C. V. Mosby Co., 1950.

Leitfaden für Prostatiker. By Prof. Dr. med. J. Minder. Stuttgart: Georg Thieme, 1950.

Sir William Osler Aphorisms from His Bedside Teachings and Writings. Collected by Robert Bennett Bean, M.D. Edited by William Bennett Bean, M.D. New York: Henry Schuman, Inc., 1950.

Lehrbuch der Roentgendiagnostik. By H. R. Schinz, W. E. Baensch, E. Friedl, E. Uehlinger. 5th rev. enl. ed. No. 2. Stuttgart: Georg Thieme; New York: Grune & Stratton, Inc., 1950.

Fortschritte der Geburtshilfe und Gynaekologie. Hormone und Vitamine und ihre Beziehung zur Gynaekologie und Geburtshilfe by Prof. W. Neuweiler, Bern. Anaesthesie und Narkose by Dr. P. Jung, St. Gallen. Zur Technik der Schmerzbekaempfung unter der normalen Geburt by Dr. O. Kaeser. Vol. 1. Basel and New York: S. Karger, 1950.